161. Paediatric epidemiology: predicting outcomes of wheeze, antenatal growth, early life exposures and outcome of premature birth

P1495

Natural history of recurrent cough in children

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Aims: Recurrent cough (RC) is common in childhood and an important cause of primary care visits. Despite that, data on the natural history of recurrent cough in unselected children are scarce.
Methods: In a population-based cohort in Leicestershire (UK) we measured recurrent cough (defined as chronic night cough + cough apart from colds + GP visits for cough) with repeated questionnaires. For non-wheezers, we computed frequency of recurrent cough at different ages, and determined predictors of RC in multivariable logistic regressions.
Results: We had data on 1247 children aged 1 year, and data on 1127, 1267, 1410, 825 aged 2, 4, 6 and 9 years respectively. Prevalence of RC at these ages was 17%, 19%, 21%, 16% and 12% respectively. Of all children with RC at age 1 year, 62% continued to report RC at age 2 years, and 46%, 35%, 28% at age 4, 6 and 9 years. Factors associated with RC at all ages were: south Asian ethnicity, chronic rhinitis and frequent snoring. Other factors associated with RC during the first 2 years of life were nursery care and posseting. In contrast, attendance to nursery care in infancy protected from RC at age 6 and 9 years. Associations with family history of atopy were marginal.
Conclusions: Recurrent cough is common and tracks strongly during childhood. At all ages, there are strong associations with upper respiratory symptoms. This might be explained by an increased susceptibility to upper respiratory infections.
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P1496

Robust prediction of later asthma in symptomatic toddlers: A novel approach

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Aim: Many children have asthma-like symptoms in early life, but few develop asthma. Several models for predicting later asthma in symptomatic toddlers have been built, but some included factors that are difficult to assess, and methods used were prone to overfitting, leading to selection or exaggeration of irrelevant factors. We aimed to identify predictors for later asthma avoiding previous limitations.
Methods: In a population-based cohort, we selected 1-3 year-olds with respiratory symptoms (current wheeze or recurrent cough) and related healthcare visits. Asthma (current wheeze and treatment) was assessed 5 years (N=1226) and 8 years (N=866) later.
The included factors are easy to assess in clinical practice: family history, symptoms at baseline, demographic and perinatal data. We used lasso penalized logistic

regression to select predictors. This minimizes the number of included predictors while maximizing area under ROC curve (AUC).
Results: Main predictors selected in the model for asthma 5 yrs later (AUC=0.76) were ≥4 wheezing attacks in the past 12mo (OR=1.65), wheeze causing breathlessness (3.1) and activity disturbance (2.4), eczema (1.5) and male sex (1.5). Other predictors (OR<1.5) were: non-viral triggers for wheeze or cough, parental history of asthma, older age at baseline and low birth weight. The results for asthma 8yrs later (AUC=0.72) were similar.
Conclusion: Among factors easy to assess in symptomatic toddlers, wheeze severity, eczema and male sex are main predictors of asthma in mid-childhood. Because our approach for variable selection avoids overfitting, the resulting prediction models should perform well with new data. However, external validation is needed.
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P1497
Phenotypes of childhood wheeze: Early symptom pattern vs. long term disease course
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Aim: Wheezing in childhood is phenotypically heterogeneous. We investigated how phenotypes defined by early symptom pattern are related to phenotypes based on later retrospective time course.
Method: We analysed data on wheeze-related symptoms (frequency and duration of episodes, shortness of breath (SOB), fever and triggers (chest infection, smoke, cold weather, "other")) in children from a population based birth cohort (ALSPAC) at ages 6m (n=2261), 18m (2400) and 30m (1786). We used latent class analysis to identify phenotypes, which were compared to previously published phenotypes based on 7 measurements of current wheeze in the first 7yrs of life (Thorax 2008;63:974–980).
Results: We identified 5 phenotypes at age 6m and 6 at ages 18m and 30m. At each age, 2 groups of severe wheezers (frequent episodes, long duration, SOB) were identified, one with episodes triggered mainly by infections and cold weather and one with "other" triggers predominating. Other phenotypes were characterised by moderate or mild symptoms and differed in patterns of triggers. Phenotypes were similar at different ages. Among children with mild wheeze, >60% were classified longitudinally as "transient early" or "prolonged early wheezers" while >34%, >46% and >63% of children in the severe groups at ages 6m, 18m, and 30m respectively were classified as "persistent wheezers".
Conclusion: In children <3yrs from the general population, severe wheeze can be associated both with a viral and a multiple trigger pattern. Severe wheeze in early childhood is a strong predictor of wheeze persisting into school age, regardless of reported triggers.
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P1498
Allergic females have the lowest chance of recovery following early wheezing
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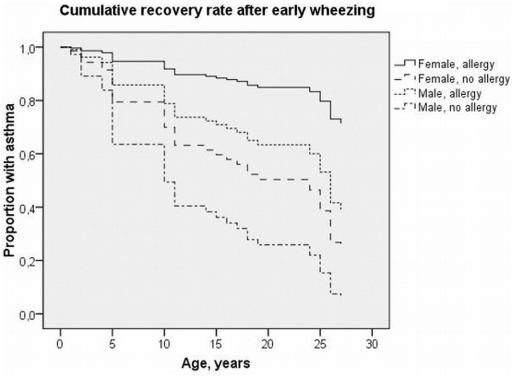
Background: We have previously reported on the outcome in childhood and adolescence in children hospitalized due to wheezing before the age of two. The aim of the present follow-up was to report on the prevalence of and risk factors for asthma at adult age.
Methods: We have prospectively studied asthma development in 101 children hospitalized due to wheezing before the age of two. The cohort was re-investigated at age 25-29 years and tested for bronchial hyper-responsiveness and allergic sensitization. The response rate at adult age was 72%.
Results: Current asthma was seen in 38% (28/73) and 50% of these had a moderate to severe asthma. In the asthmatics, symptoms triggered by exercise were reported in 79%, infection 36%, tobacco-smoke 25%, contact with pollen 32% and furred animals in 18%.



Current allergy (OR 9.8; 95% CI 2.8-34.4) and female gender (OR 3.3; 95% CI 1.1-10.3) increased the risk of adult asthma independently of each other. This is illustrated in a stratified Cox regression analysis where the females with current allergy have the lowest chance of recovery (Hazard ratio 0.1; 95% CI 0.04-0.3) compared to males without allergy.
Conclusion: In subjects hospitalized due to early wheezing, current allergy and female gender increased the risk of adult asthma. Females with current allergy had the lowest chance of recovery.

P1499
Predictors of asthma symptom remission after five years of age
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Introduction: Childhood asthma is a common condition characterised by relapse and remission. Here we sought to identify the precision of physiological measurements made in 5-year-olds for predicting asthma outcome at 10 years of age.
Methods: As part of a cohort study, 5 year old children attended a clinical assessment which included skin prick reactivity, spirometry and bronchodilator response. A respiratory symptom questionnaire was completed at ages 5 and 10 years. Children were categorised as having persistent asthma, early remittent asthma, later onset asthma or being non-asthmatic.
Results: Of the 1924 originally recruited, questionnaire data were available in 808 children at both 5 and 10 years of age including 37 with persistent asthma, 30 with early remittent asthma and 33 with later onset asthma. Skin prick reactivity was determined in 483 5-year-olds, spirometry in 410, bronchodilator response (BDR) in 164 and FE_{NO} in 110. Atopy had sensitivity of 82% [95% CI 68, 92] and specificity of 57% [95% CI 42, 68] for predicting persistent asthma in symptomatic 5–year-olds and a sensitivity of 72% [95% CI 50, 87%] and specificity of 79% [95% CI 78-80] for predicting later onset asthma in asymptomatic 5-year-olds. Regardless of asthma status at 5 years, FE_{NO} >10.7ppb had a sensitivity of 62% and specificity of 89% for asthma at 10 years. Spirometry and BDR were not predictive of later asthma outcomes
Conclusions: In this community-based cohort, objective physiological measurements taken in 5-year-olds were able to predict asthma outcome in later childhood. The absence of atopy or elevated FE_{NO} in a young child with asthma or asthma-like symptoms may be helpful in predicting low risk for future asthma symptoms.

P1500
First and second trimester fetal size and asthma outcomes at age ten years
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Introduction: Longer early fetal size is associated with reduced asthma risk and improved lung function in early childhood but outcomes in later childhood have not been reported. Here we tested the hypothesis that associations between early fetal size, asthma symptoms and lung function persist into later childhood.
Methods: In a longitudinal study, first and second trimester fetal measurements were recorded. At ten years of age a respiratory questionnaire was completed. Spirometry, bronchial challenge and skin prick testing were undertaken in a subset of children.
Results: There were 1924 individuals recruited. Fetal measurements were available in the first trimester for 903 individuals and the second trimester for 1560. Questionnaires were returned for 927 children and 449 underwent detailed phenotyping. For each mm increase in first trimester size, asthma risk reduced by 7% [95% CI 1, 13] and FEV_1 was higher by an average of 6 mls [95% CI 1, 11]. First trimester size was reduced in those with asthma at both five and ten years compared to early or late onset asthma ($p \leq 0.017$). Persistent low growth in first and second trimesters was associated with increased risk for asthma (OR 3.2 [95% CI 1.2, 8.7]) and reduced FEV_1 (mean reduction 137mls [95% CI 21, 252]) compared to persistent high growth. Fetal size was not associated with bronchial responsiveness or atopy.
Conclusions: Longer fetal size which is maintained during the first and second trimesters has an apparent protective effect on the development of persistent asthma and obstructive lung function and the underlying mechanism is independent of atopy.

P1501
Fetal and infant growth is associated with wheezing in preschool children. The Generation R study
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Background: Birth size is associated with wheezing in childhood. Not much is

known about the role of longitudinal growth in fetal life and infancy on asthma symptoms. Our aim was to examine the associations of fetal and infant growth characteristics with wheezing in preschool children.
Methods: This study was embedded in a population-based prospective cohort study among 5,125 children. Information on second and third trimester fetal growth (femur length, head circumference, abdominal circumference, fetal estimated weight) was obtained by multiple ultrasounds during pregnancy. Infant growth (length, weight) was repeatedly measured at the Community Health Centres at the ages of 3, 6, and 12 months. All growth characteristics were converted into age and sex adjusted standard deviation scores (SDS). Parental report of wheezing until the age of 4 years was yearly obtained by questionnaires.
Results: Fetal growth characteristics were not associated with wheezing at all ages. Infant weight gain was associated with the risk of wheezing in the first 2 years (Odds ratios (OR) age 1 year: 1.12 (95% Confidence Intervals (CI): 1.04, 1.22); age 2 years: 1.23 (1.12, 1.35)) per SDS weight gain in the first 3 months of life. These effect estimates were higher for children who were fetal growth restricted from the 2nd trimester to birth (age 1 year: 1.32 (1.10, 1.57), age 2 years: 1.26 (1.04, 1.54)).
Conclusions: Increased weight gain during the first 3 months after birth is associated with increased risk of wheezing in the first 2 years of life, especially after fetal growth restriction. Our results suggest that abnormal fetal and infant growth might influence the development of asthma in childhood.

P1502

Longitudinal development of lung function in extremely preterm infants

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Introduction: With the advent of modern neonatal intensive care, survival after extreme preterm (EP) birth increased considerably. Large cohorts of subjects born EP are now approaching adulthood; their lifelong pulmonary prospects being basically unknown.
Aims: To construct spirometric growth curves to early adulthood for subjects born EP.
Methods: Two area-based birth-cohorts of subjects born in 1982-85 and 1991-92 at gestational age ≤28 weeks or with birth weight ≤1000 grams (n=81) and individually matched control subjects born at term (n=74) were examined in 2001 and 2009. Paired multiple linear regression models were constructed to assess growth patterns.
Results: Most measures of lung function were significantly reduced in subjects born EP over the full study period. Mean growth of FEV1 through puberty was 1.5 liters in both preterm and control subjects, and there was a small but not significant growth from age 18 to 25.

		1991-92 cohort		1982-85 cohort	
Age (years)		10.5 (SD 0.4)	17.8 (SD 0.4)	17.7 (SD 1.2)	24.9 (SD 1.2)
FEV1 (l)*	EP	1.80 (1.68,1.92)	3.30 (3.10,3.49)	3.30 (3.02,3.58)	3.50 (3.22,3.78)
	Control	2.14 (2.05,2.24)	3.65 (3.40,3.89)	4.07 (3.81,4.31)	4.10 (3.85,4.35)
FVC (l)*	EP	2.15 (2.00,2.29)	4.09 (3,80,4.38)	3.93 (3.58,4.30)	4.47 (4.10,4.84)
	Control	2.44 (2.35,2.54)	4.22 (3.95,4.50)	4.59 (4.30,4.88)	4.92 (4.61,5.24)
FEF50 (l/sec)*	EP	2.09 (1.89,2.30)	4.06 (3.62,4.49)	3.74 (3.42,4.07)	4.01 (3.60,4.43)
	Control	2.78 (2.57,3.00)	4.79 (4.27,5.31)	5.22 (4.77,5.66)	5.44 (5.01,5.86)

*Mean values (95% CI).

Conclusions: Lung function deficits after EP birth persists to adult life. Growth in lung function was parallel in subjects born EP and at term, and no signs of age related decline was observed at age 25.

P1503

Risk factors for lower respiratory illnesses (LRI) in infants < 32 wks gestational age (GA): Do they differ by type of illness?

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Children born very preterm suffer from and are hospitalized for LRI. Risk factors for these events should be reassessed given advances in perinatal care.
All infants 22-31 wks GA born in 2003-05 in 5 Italian regions (ACTION study) were invited for pediatric assessment and telephone interview at 24 mos corrected age. Bronchiolitis/asthmatic bronchitis and bronchitis/pneumonia in previous year, and lifetime LRI hospital admissions were recorded. Parental demographics and asthma/atopy, obstetrical and perinatal variables, breastfeeding and current environmental factors (siblings, smoking/dampness at home, traffic) were assessed as possible predictors through multivariable regression analysis.
1009/1413 children had assessment+interview. Bronchiolitis/asthmatic bronchitis (18.8% of children) were significantly associated with lower GA, parental asthma (Odds ratio,OR 1.80) and day care (OR 2.00), while female sex and foreign mother were protective (OR 0.71 and 0.56). Risk of bronchitis/pneumonia (16.2%) was significantly reduced at higher GA, in twins (OR 0.45), and in infants discharged from NICU in april-september (OR 0.63). 14% of children were admitted to hospital for LRI; they were significantly more likely to have been exposed to maternal smoking in pregnancy (OR 1.67), have had birthweight <10° centile (OR 2.0) and BPD (OR 2.1); infants with LRI requiring O2 or ventilation (5.2%) had the same risk factors.
Wheezing and LRI admissions had different risk profiles: the former were similar to those in general populations studies, while the latter were associated with prenatal factors influencing lung growth (intrauterine growth restriction, smoke) and BPD.

P1504

Preterm birth and inhaled corticosteroid usage in 6-19-year-olds – A Swedish national cohort study

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Objective: Preterm birth is associated with respiratory morbidity later in life, including asthma. Previous studies have mainly focused on asthma in early childhood in children born extremely preterm. In this study we examined the risk of asthma in a national cohort of school children by degree of immaturity expressed as completed gestational weeks at birth.
Methods: Register study in a Swedish national cohort of 1 100 826 children 6-19 years old. Retrieval of at least one prescription of inhaled corticosteroids (ICS) during 2006 was used as our main indicator for asthma. Logistic regression was used to test hypotheses with adjustment for multiple socio-economic and perinatal indicators.
Results: Degree of immaturity, expressed as completed gestational weeks at birth, had an inverse dose-response relationship with ICS usage. Compared to children born between 39 and 41 weeks gestation, the odds ratio for ICS usage increased with the degree of prematurity, from 1.10 (1.08-1.13) for children born in weeks 37-38, to 2.28 (1.96-2.64) for children born in weeks 24-28, after adjustment for socio-economic confounders and perinatal mediators.
The increase in ICS usage with decreasing gestational age at delivery was similar in boys and girls and declined with older age.
Conclusion: Preterm birth increases the risk of ICS usage in 6-19 year olds by degree of immaturity, all the way from extremely preterm to early term birth.

P1505

Early life antecedents of persistent wheeze in young adults

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Introduction: Factors present in infancy have been associated with respiratory outcomes in childhood. Risk factors for wheeze in adults differ from those in children, for example female gender and active smoking. Here we test the hypothesis that physiological outcomes measured in infancy are associated with persistent respiratory outcomes in eighteen year olds.
Methods: As part of a longitudinal birth cohort study, measurements of infant lung function and atopy were made in infancy. Participants were followed up with at ages 6, 12 and 18 years. Based on reported symptoms, individuals were categorised as remittent wheeze, later onset wheeze, persistent wheeze and no wheeze.
Results: Of the 253 individuals originally recruited, 148 were followed up at age 18 years including 13 with persistent wheeze, 13 with remittent wheeze, 23 with later onset wheeze and 99 with no wheeze. Compared to the no wheeze group, persistent wheeze was independently associated with reduced lung function at one month (mean reduction% predicted V'maxFRC 43 [95% CI 13, 74]), increased length at one month (40% increase risk per cm increase [95%CI 6, 187]), atopy in infancy (OR 5.2 [95%CI 1.1, 23.8]) and current smoking (OR 6.1 [95%CI 1.3, 27.0]). Later onset wheeze was associated with female sex (OR 4.0 [95% CI 1.5, 11.4]). Remittent wheeze was not associated with the risk factors considered in the analysis.
Conclusion: Although female sex and active smoking are risk factors for wheeze in adulthood, the presence of reduced lung function and atopy in infancy remain risk factors for ongoing respiratory symptoms in young adults.

P1506

Factors associated to an earlier wheezing episode during the first year of life in Europe and Latin America: The EISL study

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Background: There is scarce information about what factors might influence the time to the first wheezing episode in infants.
Methods: The "Estudio Internacional de Sibilancias en Lactantes (EISL)" included 13,684 infants who wheezed at least once in the first year of life, recruited from 13 centres in 6 Latin American countries (n=12,045) and from 5 centres in 2 European countries (n=1,639). A multivariate Cox regression analysis was performed using as dependent variable the time to the first wheezing episode. The regression included the following factors: gender, parental asthma or rhinitis, infant eczema, mother smoking in pregnancy, cold(s) in the first 3 mo, nursery school, breast feeding >= 3 mo, number of siblings, persons at home, mould stains on walls, university studies of mother, Afro-American ethnicity, and pets at home. An adjusted hazard ratio (aHR) of the pooled whole population and also separately for EU and LA was calculated.
Results:

Adjusted hazard ratios (aHR) for an earlier episode of wheezing in the frist year of life

	Whole population		Latin America		Europe	
	aHR	95%CI	aHR	95%CI	aHR	95%CI
Cold(s) during the 1st 3 months	1.84	1.77–1.91	1.85	1.78–1.92	1.85	1.66–2.06
Breast feeding >3 months	0.93	0.90–0.97	0.93	0.90–0.97	0.98	0.88–1.09
Mould stains on hosehold walls	1.04	1.00–1.08	1.05	1.00–1.09	1.12	0.95–1.32
University studies in mother	0.99	0.96–1.03	0.99	0.95–1.04	0.82	0.71–0.95
Infant eczema	1.02	0.98–1.05	1.01	0.97–1.05	1.25	1.10–1.43

Conclusions: Some factors usually shown to be a risk factor for wheezing are not associated to a shorter period of time to the first episode. Furthermore, some delaying or advancing factors are different in Europe as compared to Latin America.

P1507

Long-term evolution of virus-induced and multi-trigger wheeze in children of the EGEA study

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Background: Recent guidelines have proposed different phenotypes according to triggers (episodic/virus (EVW) and multiple trigger wheeze (MTW)) in preschool children. Studies aimed at characterizing asthma evolution according to these phenotypes are seldom.
Aims: To investigate lung function and asthma evolution up to adulthood between MTW and EVW in childhood.
Methods: 588 children, aged 10.9±3.0 years included in EGEA study were classified as non wheezer (n=265), EVW (wheeze only with viral infections and asymptomatic between episodes, n=131) and MTW (wheeze with viral infections and between episodes with triggers such as dust, tobacco smoke, exercise, and cold air, n=192). 139 (72.4%) MTW and 85 (64.9%) EVW participated to the 12-year follow-up.
Results: At baseline MTW were older (11.5 vs 10.1 years), more atopic (at least 1 positive skin test, 89.7 vs 57.0%), had more often active asthma (symptoms or treatment in the past year, 96.2 vs 58.3%) and ICS use in the past year (54.7 vs 26.4%) compared to EVW. FEV_1 and FVC (% pred Stanojevic) were similar in both groups but MTW had lower FEV_1/FVC ratio (85.4±7.1vs 88.3±7.0, p= 0.001) and FEF_{25-75} (93.6±25.5 vs 103.2±26.5%, p=0.002) compared to EVW. At follow-up MTW had more often active asthma (71.9 vs 38.5%, p=0.003), and ICS use (39.1 vs 18.1%) compared to EVW. FEV_1/FVC and FEF_{25-75} remained lower in MTW than in EVW (81.2±7.6 vs 84.8±7.8%, p=0.002 and 94.6±25.5 vs 110.3±26.8%, p<0.0001 respectively).
Conclusions: Our results suggest that the episodic vs multi-trigger wheeze classification applied in school-age children identified groups of wheezers with different baseline characteristics and long-term evolution.

P1508

Determinants of lung function and bronchodilator response in 4-year-old children

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Objectives: The aim of this study was to investigate which early life factors are associated with baseline lung function and the change after bronchodilation in 4-year-old children.
Methods: Environmental and health information on children involved in a Belgian prospective birth cohort (PIPO) were collected from birth on using bi-annual questionnaires. At 1 and 4 years of age, a blood sample was analysed for specific IgE. At 4 years of age, baseline and post-bronchodilator respiratory resistance at 6 Hz (R6) was obtained with the forced oscillation technique. Potential determinants were selected based on literature and univariate analyses. Response variables were transformed to allow for the normal distribution assumption. Model reduction on the initial multiple linear regression models was performed by stepwise backward elimination based on the 95% confidence level.
Results: Baseline and post-bronchodilator R6 data were obtained in 535 and 501 children, respectively. Results are regression coefficient B with standard error. Current height (-0.017 (0.004)) and weight of the child (0.015 (0.008)), maternal asthma (0.108 (0.047)), lower respiratory tract infections (0.064 (0.025)) and atopy against cat at the age of 1 year (0.236 (0.085)) were significant determinants of the baseline R6 value. Interestingly, other determinants were observed for ΔR6, namely parental educational level (-0.080 (0.041)), pre-and postnatal smoke exposure (0.158 (0.067)), lower respiratory tracts infections (0.075 (0.027)) and atopy against dog at 1 year of age (0.311 (0.124)).
Conclusion: In 4-year-old children different determinants for the baseline respiratory resistance and the bronchodilator response were observed.

P1509

Indoor endotoxin and respiratory symptoms in urban schoolchildren

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Background and aim: Endotoxin is a marker of microbial exposure and rural studies suggested it is negatively co-related with asthma. This study aims to determine the relationship of indoor endotoxin and manifestations of respiratory symptoms in urban children in Hong Kong.
Methods: Random sample of schoolchildren aged 7 to 11 years were recruited through the school system. Parents completed the locally validated ISAAC questionnaire with additional questions about the home environment. Random subgroup of subjects was recruited for SPTs and dust samples were collected according to the ISAAC Phase II protocol. Endotoxin levels were log-transformed before analysis.
Results: 3,546 primary schoolchildren were screened with a participation rate of 96%. A random subsample of 1,303 subjects has been skin-tested with 439 also provided mattress dust samples. Among them, 37 (8.4%) had at least one wheezing attack in the past year and 47 (10.7%) had a physician diagnose of asthma. The median (interquartile range) of endotoxin concentration (EU/mg) and load (EU/m^2) were 12.9 (6-25) and 547 (230-1,137) in those without current wheeze; they were 34 (19-83) and 1,689 (853-3,301) in those with current wheeze. The differences were significantly different ($p< 0.01$) adjusted for confounders. Among those with a asthma diagnosis, higher endotoxin level was associated with use of asthma medication in the past year.
Conclusion: Higher level of endotoxin level in this urban sample of schoolchildren is associated with wheezing and increased use of asthma medication among known asthmatics. Further studies are needed to reveal the possible roles of microbial exposure in affecting the development of asthma in urban and rural settings.

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Does maternal smoking play a role as an inducer, rather than trigger, of asthma and respiratory symptoms?

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Background: Asthma is a complex chronic disease arising from the interaction of genetic and environmental factors. In children, it is difficult to separate any role of maternal smoking in the antenatal induction of asthma from a later role as a symptom trigger, as most mothers who smoke in pregnancy continue to smoke after their child's birth.
Aim: To estimate the association between parental smoking and asthma and respiratory symptoms in adults, and to compare findings with those for current exposure to environmental tobacco smoke (ETS).
Methods: The Midspan Family Study included offspring aged 30-59 years, whose parents reported their smoking habits as part of an epidemiological study 20 years earlier. Offspring completed a questionnaire and underwent spirometry. We used

logistic regression to estimate the association between parental smoking or current ETS and asthma and symptoms in 985 lifelong non-smokers.
Results: Maternal smoking was associated with wheeze, wheeze without a cold, wheeze with breathlessness, current asthma, ≥3 asthma symptoms, odds ratios (95% confidence intervals) after adjustment for covariates: 2.1 (1.3-3.4), 2.5 (1.4-4.7), 2.9 (1.6-5.2), 2.2 (1.1-4.1), 2.6 (1.5-4.6) respectively. There were dose-response associations for all five outcomes. There was no evidence of association between maternal smoking and breathlessness or chronic sputum, or between paternal smoking and asthma or any symptom. Current ETS was positively associated with wheeze variables, current asthma, ≥3 asthma symptoms, breathlessness and chronic sputum.
Conclusions: Maternal smoking, probably in-utero, plays a role in the induction of phenotype(s) related to wheeze and asthma in adults.

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Microbial markers and the development of asthma in childhood: A birth cohort study
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Background: Early-life exposure to environmental microbial agents may be associated with a development of asthma.
Objective: To determine the effect of microbial exposure at homes in early age on the risk of asthma.
Methods: A birth cohort of 396 children was followed-up with questionnaires until the age of 5 years. Collection of living room floor dust samples and home inspection for moisture damage were performed before the age of 1 year. Concentrations of 3-hydroxy fatty acids (3-OH FAs), muramic acid, ergosterol and quantitative polymerase chain reaction (qPCR) for two bacterial genera and six fungal species, genera or groups were determined from house dust.
Results: The associations between early microbial exposure and occurrence of doctor-diagnosed asthma were mainly seen with concentrations of 3-OH FAs, qPCR for *Mycobacterium* and *Wallemia sebi*, and amount of dust. Significant interaction was observed between major moisture damage in home and 3-OH FAs ($p=0.006$). In addition, there was a suggestion ($p\leq0.15$) that 3-OH FAs and qPCR for *Mycobacterium* were inversely associated with asthma especially among non-farm children.
Conclusion: The study results suggest that microbial markers may represent different types of microbial exposure in different environments e.g. living on a farm or in a moisture damaged house. The source and variety of microbial exposures should be better taken into account in future studies on the development of asthma.