

Formulation of the theoretical design

This document contains the extracted information for 30 out of the 66 articles included in the methodological review. It concerns here the 20 most recent articles (2015-2018) and 10 older articles (2005-2008). For every article we formulated a theoretical design which is written underneath the extracted information.

Overview extracted information from articles:

1. # (number of the article in the full table)
2. Reference (author)
3. Journal
4. Year of publication (YOP)
5. Impact factor (IF)
6. Title
7. Aim of the study
8. Domain and location in text
9. Outcome author
10. Measure of frequency for the outcome
11. Exposure author
12. Operationalization exposure
13. Measurement method exposure
14. Do the authors mention "(study) design" and where?
15. Design of data collection (and where in text)
16. Design of data analysis
17. Measure of association (place in text & operationalization)
18. T0 (baseline, implicitly or explicitly mentioned?)
19. Confounders
20. Effect modifiers
21. Justification for the selection of confounders or effect modifiers
22. Referral to reporting guideline or theoretical work?

The theoretical design is formulated for every study. Sometimes two theoretical designs are possible, and in that case we mentioned them both in this document. We then selected the one which was the most inclusive (in bold and underlined).

List of abbreviations:

| | |
|--------|--|
| ABX | Antibiotics |
| BMI | Body Mass Index |
| ETS | Environmental tobacco smoke |
| HR | Hazard ratio |
| ICD | International classification of disease |
| ICS | Inhaled corticosteroids |
| ISAAC | International Study on Asthma and Allergies in Childhood |
| LRTI | Lower respiratory tract infection |
| NSAIDs | Non-steroidal anti-inflammatory drugs |
| OR | Odds ratio |
| RR | Rate ratio |
| RTI | Respiratory tract infection |
| SES | Socio economic status |
| URTI | Upper respiratory tract infection |
| UTI | Urinary tract infection |

1. The effect of breastfeeding on the risk of asthma in high-risk children: a case-control study in Shanghai, China. Huo et al.

| | |
|--|---|
| Number | 1 |
| Reference | Huo et al. |
| Journal | BMC pregnancy and childbirth |
| YOP | 2018 |
| IF | 2.3 |
| Title | The effect of breastfeeding on the risk of asthma in high-risk children: a case-control study in Shanghai, China |
| Aim | <i>"...to investigate the association between ABX use in pregnancy and the risk of childhood asthma, and the possible role of breast feeding in modulating the risks..."</i> |
| Domain | Children aged 3 to 12 years old (methods) |
| Outcome | Childhood asthma |
| Measure of frequency | / |
| Exposure | Maternal ABX use in pregnancy |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Face-to-face interview |
| "(Study) design"? | Yes (methods & discussion) |
| Data collection design | Case-control study (title and abstract) Hospital-based case-control study (methods and discussion) Retrospective study (discussion) |
| Data analysis design | Multiple logistic regression |
| Measure of association | OR (statistical analysis methods, categorical) |
| T0 | At 6 months of age (referred to as baseline, explicitly) |
| Confounders | Maternal age at delivery; maternal education level; child's age (not specified); child's gender; gestational age at birth; delivery mode; feeding status first 6 months of life (exclusive breastfeeding: yes/no); family history (allergic disorder: yes/no/unknown) |
| Effect modifiers | Child's age (not specified); child's gender; feeding status first 6 months of life (exclusive breastfeeding: yes/no); family history (allergic disorder: yes/no/unknown) |
| Justification selection confounders/effect modifiers? | yes: previous publications |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset as a function of baseline (at 6 months of age) exposure profile (**maternal ABX exposure during pregnancy**) in **children aged 3 to 12 years** adjusted for confounding by maternal age at delivery, delivery mode, child's gender, gestational age at birth, family history (allergic disorder: yes/no/unknown), maternal educational level, feeding status first 6 months of life (exclusive breastfeeding: yes/no), child's age (not specified) and for effect modification by child's gender, family history (allergic disorder: yes/no/unknown), feeding status first 6 months of life (exclusive breastfeeding: yes/no) and child's age (not specified).

2. Effects of antibiotics on the development of asthma and other allergic diseases in children and adolescents. Do Hyun Kim et al.

| | |
|--|---|
| Number | 2 |
| Reference | Do Hyun Kim et al. |
| Journal | Allergy Asthma Immunol Res |
| YOP | 2018 |
| IF | 3.8 |
| Title | Effects of antibiotics on the development of asthma and other allergic diseases in children and adolescents |
| Aim | <i>"...determine if the duration of exposure to ABX in children and adolescents is associated with the later development of allergic disease."</i> |
| Domain | Children and adolescents (title, introduction, methods, results & discussion) |
| Outcome | Asthma diagnosis |
| Measure of frequency | Incidence |
| Exposure | Duration of ABX exposure 7 years prior to development of allergic disease |
| Operationalization exposure | Annual average ABX prescription days (6 categories) |
| Measurement exposure | National Health Insurance (NHIS) database |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Cross-sectional study (discussion) |
| Data analysis design | Multiple logistic regression |
| Measure of association | OR (tables and figures, 6 categories) |
| T0 | Onset asthma (the day allergic diseases were first diagnosed was set as an index date) or before the last day of 2015 (for controls) (explicitly) |
| Confounders | Age (at asthma diagnosis or inclusion as control); gender; number of days on which healthcare providers were visited (not specified when); income (insurance premium at onset asthma or before the last day of 2015); place of residence (at onset asthma or before the last day of 2015) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current incidence of asthma onset as a function of baseline (asthma onset) exposure profile (**exposure to ABX 7 years prior to the development of asthma**) in **children and adolescents** adjusted for confounding by age (at asthma diagnosis or inclusion as a control), gender, number of days on which healthcare providers were visited (not specified when), income (insurance premium at onset asthma or before the last day of 2015), place of residence (at onset asthma or before the last day of 2015).

3. The current prevalence of asthma, allergic rhinitis, and eczema related symptoms in school-aged children in Costa Rica. Soto-Martínez et al.

| | |
|--|---|
| Number | 3 |
| Reference | Soto-Martínez et al. |
| Journal | J asthma |
| YOP | 2018 |
| IF | 2.0 |
| Title | The current prevalence of asthma, allergic rhinitis, and eczema related symptoms in school-aged children in Costa Rica |
| Aim | <i>"...to study the current prevalence 12 years later in an inner-city group of children between 6 and 13 years old."</i> |
| Domain | Children 6-13 years old (title, introduction, methods & discussion) |
| Outcome | Diagnosis of asthma (wheezing or whistling in the chest in the previous 12 months) |
| Measure of frequency | Prevalence |
| Exposure | ABX use in the first 12 months of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | ISAAC questionnaires at 6-13 years of age |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Cross-sectional study (abstract, discussion & conclusion) |
| Data analysis design | Poisson regression Multivariable analysis |
| Measure of association | OR (1 OR) |
| T0 | Onset asthma (implicitly) |
| Confounders | Complete set of confounders not specified, table 1 and table 3 include possibly a couple of confounders: rhinitis (ever); rhinitis (12 months before onset asthma); rhinoconjunctivitis (in the last 12 months); eczema (yes/no, last 12 months); acetaminophen use (yes/no, first 12 months of life); traffic next to house (not specified); family member smoking at home (during the first year of life); wheezing chest after exercise (last 12 months); dry cough at night (last 12 months) |
| Effect modifiers | Complete set of effect modifiers not specified, table 1 and table 3 include possibly a couple of effect modifiers: rhinitis (ever); rhinitis (12 months before onset asthma); rhinoconjunctivitis (in the last 12 months); eczema (yes/no, last 12 months); acetaminophen use (yes/no, first 12 months of life); traffic next to house (not specified); family member smoking at home (during the first year of life); wheezing chest after exercise (last 12 months); dry cough at night (last 12 months) |
| Justification selection confounders/effect modifiers? | Explanation on how to check for confounding and effect modification in statistical analysis part |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma as a function of baseline exposure (asthma onset) profile (**ABX use in the first 12 months of life**) in **children aged 6-13 years of age** adjusted for confounding by rhinitis (ever), rhinitis (12 months before onset asthma), rhinoconjunctivitis (in the last 12 months), eczema (yes/no, last 12 months), acetaminophen use (yes/no, first 12 months of life), traffic next to house (not specified), family member smoking at home (during the first year of life), wheezing chest after exercise (last 12 months), dry cough at night (last 12

months) and effect modification by rhinitis (ever), rhinitis (12 months before onset asthma), rhinoconjunctivitis (in the last 12 months), eczema (yes/no, last 12 months), acetaminophen use (yes/no, first 12 months of life), traffic next to house (not specified), family member smoking at home (during the first year of life), wheezing chest after exercise (last 12 months), dry cough at night (last 12 months).

COMMENT: results section – B, theoretical design here: Prevalence of past exposure to antibiotics in the first 12 months of life as a function of current asthma status

4. Prenatal antibiotic exposure and childhood asthma: a population-based study. Loewen et al.

| | |
|---|---|
| Number | 4 |
| Reference | Loewen et al. |
| Journal | Eur Respir J |
| YOP | 2018 |
| IF | 12.2 |
| Title | Prenatal antibiotic exposure and childhood asthma: a population-based study |
| Aim | <i>"...examining the association of maternal ABX use and childhood asthma..."</i> |
| Domain | Children (Introduction & methods) |
| Outcome | Child asthma = asthma after the age of 5: any hospitalization for asthma or at least 2 physician diagnosed asthma (at least 3 months apart and within 1 year) or at least 2 asthma medication prescriptions within 1 year |
| Measure of frequency | Incidence rate |
| Exposure | Maternal ABX use during pregnancy |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | From database (prescriptions) |
| "(Study) design"? | Yes (methods) |
| Data collection design | Retrospective cohort study (methods) Population-based cohort study (discussion & abstract) |
| Data analysis design | Time-to-event analysis Cox regression |
| Measure of association | HR Incidence rate |
| T0 | Birth child (implicitly) |
| Confounders | Residence location (at birth); length of gestation (at birth); number of siblings (at birth); SES (at birth); infant gender; maternal asthma (at birth child); postnatal ABX exposure first year of life |
| Effect modifiers | Infant gender; method of birth; newborn feeding method |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset as a function of baseline (at birth) exposure profile (maternal ABX use during pregnancy) in children adjusted for confounding by residence location (at birth), length of gestation (at birth), number of siblings (at birth), SES (at birth), infant gender, maternal asthma (at birth child), postnatal ABX exposure first year of life and effect modification by infant gender, method of birth and newborn feeding method.

5. Effect of antibiotic use for acute bronchiolitis on new-onset asthma in children. Lun-chen et al.

| | |
|--|---|
| Number | 5 |
| Reference | Lun-chen et al. |
| Journal | Scientific Reports |
| YOP | 2018 |
| IF | 4.1 |
| Title | Effect of antibiotic use for acute bronchiolitis on new-onset asthma in children |
| Aim | <i>"...to assess the relationship of early life ABX use for bronchiolitis with new-onset asthma in children."</i> |
| Domain | Children with a history of acute bronchiolitis in the first 2 years of life (title, introduction & discussion) |
| Outcome | New-onset asthma: ICD 9 criteria AND receipt of selective B2-agonist and/or ICS treatment twice within 1 year (age2-18) |
| Measure of frequency | / |
| Exposure | ABX dosage: ABX prescriptions (at least one ABX in the 5 years before the onset of asthma) |
| Operationalization exposure | Cumulative defined daily dose (DDD) (3 categories) Dichotomous (Yes/No) |
| Measurement exposure | Outpatient prescription database |
| "(Study) design"? | No |
| Data collection design | Matched case-control study (results) |
| Data analysis design | Conditional logistic regression |
| Measure of association | OR (methods, OR per category of ABX exposure) |
| TO | Asthma onset (implicitly) |
| Confounders | urban residence (not specified); allergic rhinitis (not specified); atopic dermatitis (not specified); chronic rhinitis (not specified); age (at inclusion); acute sinusitis (not specified); gastroesophageal reflux (not specified); use of NSAIDs 120 days before asthma onset; gender; subtype of antibiotics (first 2 years of life) |
| Effect modifiers | age-stratified analysis |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current incidence of asthma onset as a function of baseline (asthma onset) exposure profile (ABX use for acute bronchiolitis in the 5 years before the onset of asthma) in children with a history of acute bronchiolitis in the first 2 years of life adjusted for confounding by age (at inclusion), subtype of antibiotics (5 years prior to the onset of asthma), allergic rhinitis (not specified), atopic dermatitis (not specified), chronic rhinitis (not specified), acute sinusitis (not specified), gastroesophageal reflux (not specified), urban residence (not specified), use of NSAIDs (120 days before asthma onset), gender and effect modification by age.

6. Association between use of acid-suppressive medications and antibiotics during infancy and allergic diseases in early childhood. Mitre et al.

| | |
|--|---|
| Number | 6 |
| Reference | Mitre et al. |
| Journal | JAMA Pediatrics |
| YOP | 2018 |
| IF | 10.8 |
| Title | Association between use of acid-suppressive medications and antibiotics during infancy and allergic diseases in early childhood |
| Aim | <i>"...to evaluate the hypothesis that exposure to either acid-suppressive medications or ABX during infancy is associated with an increased risk of childhood allergic disease..."</i> |
| Domain | Early childhood (introduction, methods, results & discussion) |
| Outcome | Asthma: after the age of 6 months (ICD) |
| Measure of frequency | Incidence |
| Exposure | ABX prescription at any time prior to the age of 6 months |
| Operationalization exposure | Categorical (cut off 10 days) |
| Measurement exposure | MHS (Tricare Management Activity Military Health System) prescription database |
| "(Study) design"? | Yes (abstract) |
| Data collection design | Retrospective cohort analysis (introduction) Retrospective cohort study (methods & discussion) |
| Data analysis design | Cox proportional hazards regression |
| Measure of association | HR (one hazard ratio, time-to-event analysis, methods) |
| T0 | At 6 months of age (implicitly) |
| Confounders | Prematurity; gender; caesarean delivery; other drug classes (first 6 months of life) |
| Effect modifiers | Any significant first order interaction terms; interaction with time |
| Justification selection confounders/effect modifiers? | Yes: publication on taking into account interaction with time |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset after the age of 6 months as a function of baseline (at 6 months of age) exposure profile (ABX use at any time prior to the age of 6 months) in early childhood adjusted for confounding by prematurity, gender, caesarean delivery, other drug classes (first 6 months of life) and effect modification by any significant first order interaction terms (not specified) and time.

7. Prenatal and early-life antibiotic use and risk of childhood asthma: a retrospective cohort study. Yoshida et al.

| | |
|--|---|
| Number | 7 |
| Reference | Yoshida et al. |
| Journal | Pediatr Allergy Immunol |
| YOP | 2018 |
| IF | 4.1 |
| Title | Prenatal and early-life antibiotic use and risk of childhood asthma: a retrospective cohort study |
| Aim | <i>"...evaluate the association between ABX exposure in early life and asthma development in childhood considering the types of ABX..."</i> |
| Domain | Children up to the age of 6 years (methods) |
| Outcome | Incidence of asthma: up to age 6 (diagnosis ICD & ICS and controllers use) (at 12-35 months and 36-72 months of age) |
| Measure of frequency | Incidence |
| Exposure | Prescription of ABX to the mother during pregnancy or the child during the first year of birth |
| Operationalization exposure | Dichotomous (Yes/No) Type of ABX (4 categories) Number of ABX prescriptions (3 categories) |
| Measurement exposure | Large-scale claim database |
| "(Study) design"? | Yes (introduction & methods) |
| Data collection design | Retrospective study (abstract) Retrospective cohort study (title & methods) |
| Data analysis design | Cox proportional hazards regression |
| Measure of association | HR (for every category of exposure) |
| T0 | At 12 months of age (explicitly) |
| Confounders | Gender; familial factors (by sibling analysis) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | Yes: (9, 12) referred to studies using the same design to adjust for confounding |
| Reporting guideline or theoretical work? | No |

Theoretical design:

The future incidence of asthma onset as a function of baseline (at 12 months of age) exposure profile (maternal exposure to ABX during pregnancy/Abx exposure in the first year of life) in children up to the age of 6 years adjusted for confounding by gender and familial factors (by sibling analysis).

8. Antibiotics in the first week of life were associated with atopic asthma at 12 years of age. Strömberg et al.

| | |
|--|--|
| Number | 8 |
| Reference | Strömberg et al. |
| Journal | Acta Paediatrica |
| YOP | 2018 |
| IF | 2.6 |
| Title | Antibiotics in the first week of life were associated with atopic asthma at 12 years of age |
| Aim | <i>"...to examine the prevalence and risk factors for asthma at 12 years and to examine associations with atopic asthma and non-atopic asthma. In particular we wanted to analyze whether the long-term effects of ABX during the first week of life could be seen at age 12."</i> |
| Domain | Children 12 years of age (methods) |
| Outcome | 'Current' asthma at age 12 years: Atopic 'current' asthma at age 12 Non-atopic 'current' asthma at age 12 |
| Measure of frequency | Prevalence |
| Exposure | ABX treatment in the first week of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Questionnaire at 6 months of age |
| "(Study) design"? | No |
| Data collection design | Prospective birth cohort study (discussion) Follow-up study (discussion) |
| Data analysis design | Multivariate logistic regression |
| Measure of association | OR (methods) |
| T0 | 1 year of age/12 years of age (implicitly) |
| Confounders | maternal smoking during pregnancy; being born at <37 weeks gestation; any breast feeding for 4 months or longer; parental levels of education; parental asthma; being born small for gestational age; caesarian section; doctors-diagnosis of food allergy (first year of life); parental rhinitis, parental eczema; gender; maternal medication (during pregnancy); recurrent wheeze (first year of life); introduction of egg before 9 months of age; introduction of fish before 9 months of age; fish once a month or more in infancy; damp mould in the home (at 6 months of age); cat at home during infancy |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Current prevalence of asthma ('current'/atopic 'current'/ non-atopic 'current') as a function of baseline (12 years of age) exposure profile (**ABX exposure in the first week of life**) in **children 12 years of age** adjusted for confounding by maternal smoking during pregnancy, being born at <37 weeks gestation, any breast feeding for 4 months or longer, parental levels of education, parental asthma, being born small for gestational age, caesarian section, doctors-diagnosis of food allergy (first year of life), parental rhinitis, parental eczema, gender, maternal medication (during pregnancy), recurrent wheeze (first year of life),

introduction of egg before 9 months of age, introduction of fish before 9 months of age, fish once a month or more in infancy, damp mould in the home (at 6 months of age) and cat at home during infancy.

Future prevalence of asthma ('current'/atopic 'current'/ non-atopic 'current') as a function of baseline (at 1 year of age) exposure profile (ABX exposure in the first week of life) in children 12 years of age adjusted for confounding by maternal smoking during pregnancy, being born at <37 weeks gestation, any breast feeding for 4 months or longer, parental levels of education, parental asthma, being born small for gestational age, caesarian section, doctors-diagnosis of food allergy (first year of life), parental rhinitis, parental eczema, gender, maternal medication (during pregnancy), recurrent wheeze (first year of life), introduction of egg before 9 months of age, introduction of fish before 9 months of age, fish once a month or more in infancy, damp mould in the home (at 6 months of age) and cat at home during infancy.

9. Influence of antibiotic use in early childhood on asthma and allergic diseases at age 5.
Yamamoto-Hanada et al.

| | |
|--|---|
| Number | 9 |
| Reference | Yamamoto-Hanada et al. |
| Journal | Ann Allergy Asthma Immunol |
| YOP | 2017 |
| IF | 3.2 |
| Title | Influence of antibiotic use in early childhood on asthma and allergic diseases at age 5 |
| Aim | <i>"...to elucidate the relation between postnatal ABX exposures within the first two years of life and allergic disease in children at 5 years of age..."</i> |
| Domain | Children 5 years of age (introduction & discussion) |
| Outcome | 'Current' asthma (past 12 months) at 5 years of age |
| Measure of frequency | / |
| Exposure | History of ABX use (antibiotics ever in the first 2 years of life) and types of ABX used |
| Operationalization exposure | Dichotomous (Yes/No) Classes of ABX (4 categories) |
| Measurement exposure | Questionnaire at 2 years of age |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Hospital-based prospective birth cohort study (methods) |
| Data analysis design | Multivariate logistic regression |
| Measure of association | OR (per category of exposure, methods) |
| T0 | At 2 years of age (implicitly) |
| Confounders | maternal history of allergy; maternal age at pregnancy; maternal smoking during pregnancy; mode of delivery; gestational age at delivery; daycare attendance (during the first 2 years of life); number of previous live births; bronchitis (at 2 years of age); gender |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future prevalence of 'current' asthma as a function of baseline (at 2 years of age) exposure profile (use of ABX in the first two years of life) in children 5 years of age adjusted for confounding by maternal history of allergy, maternal age at pregnancy, maternal smoking during pregnancy, mode of delivery, gestational age at delivery, daycare attendance (during the first 2 years of life), number of previous live births, bronchitis (at 2 years of age) and gender.

10. Early life antibiotic use and the risk of asthma and asthma exacerbations in children.
Ahmadizar et al.

| | |
|--|---|
| Number | 10 |
| Reference | Ahmadizar et al. |
| Journal | Pediatr Allergy Immunol |
| YOP | 2017 |
| IF | 4.1 |
| Title | Early life antibiotic use and the risk of asthma and asthma exacerbations in children |
| Aim | <i>"...evaluate the effect of early life ABX use on the risk of asthma onset later in life in the general population. Moreover, in the pediatric population with asthma, the association between early life ABX use and the risk of asthma exacerbations later in life was studied."</i> |
| Domain | Children (Generation R and Seaton) Children with asthma (Pacman and Breathe) |
| Outcome | Physician diagnosed asthma and asthma exacerbations: Generation R: ever asthma? Confirmed by doctor? (age 9-10) Seaton: ever asthma? Confirmed by doctor? (age 10) PACMAN: asthma exacerbations in the past 12 months (age 4-12 years) (emergency department visits, oral corticosteroids) BREATHE: : asthma exacerbations in the past 6 months (age 3-19 years) |
| Measure of frequency | Prevalence rate Cumulative incidence rate |
| Exposure | Antibiotics use (all 4 cohorts) Timing of ABX use (Generation R, Pacman and Breathe) Number of prescriptions during first 3 years of life (Pacman and Breathe) Total days of exposure to ABX in the first 3 years of life (Pacman and Breathe) |
| Operationalization exposure | Dichotomous (exposed vs. never exposed) Timing first ABX use (1st, 2nd, 3rd year of life) (GENERATION R, PACMAN & BREATHE) Number of prescriptions during first 3 years (PACMAN & BREATHE) (and total days of exposure) |
| Measurement exposure | Generation R: parental questionnaire at 1, 2 and 3 years Seaton: first 6 months parent-reported Pacman & Breathe: pharmacy data from first year of life |
| "(Study) design"? | Yes (methods & discussion) |
| Data collection design | 2 population based cohorts (abstract & methods) 2 asthma cohorts (abstract) |
| Data analysis design | Multivariable logistic regression Meta-analysis |
| Measure of association | OR (methods, OR per category of ABX exposure) |
| T0 | Generation R: at 1 year of age Seaton: at 6 months of age Pacman & Breathe: asthma onset (implicitly) |
| Confounders | Generation R, Pacman and Breathe: age (not specified); gender; family history of asthma or allergy Seaton: gender; family history of asthma or allergy |
| Effect modifiers | Age-stratified analysis |
| Justification selection confounders/effect modifiers? | No, based on available variables in the database |

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| Reporting guideline or theoretical work? | No |
|--|----|

Theoretical design:

Generation R:

Future prevalence of asthma as a function of baseline (at 1 year of age) exposure profile (ABX use ever/ABX use in the first year of life/2nd year of life/3rd year of life) in children adjusted for confounding by age (not specified), gender, family history of asthma or allergy and effect modification by age.

Seaton:

Future prevalence of asthma as a function of baseline (at 6 months of age) exposure profile (ABX use ever/ABX use in the first 6 months of life) in children adjusted for confounding by, gender and family history of asthma or allergy.

Pacman & Breathe:

Future prevalence of asthma exacerbations as a function of baseline (asthma onset) exposure profile (ABX use in the first 3 years of life) in children with asthma adjusted for confounding by age (not specified), gender, family history of asthma and effect modification by age.

11. Evaluation of the associations between childhood asthma and prenatal and perinatal factors. Kashanian et al.

| | |
|--|--|
| Number | 11 |
| Reference | Kashanian et al. |
| Journal | Int J Gynecol Obstet |
| YOP | 2017 |
| IF | 2.0 |
| Title | Evaluation of the associations between childhood asthma and prenatal and perinatal factors |
| Aim | <i>"...to identify prenatal and perinatal risk factors of childhood asthma."</i> |
| Domain | Children aged 7-14 years (methods) |
| Outcome | Diagnosis of asthma (age 7-14 years) |
| Measure of frequency | / |
| Exposure | Not specified in methods In tables: ABX during pregnancy |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Maternal data sheets from hospitals where children were delivered |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Retrospective case-control study (abstract & methods) |
| Data analysis design | Forward logistic regression Multivariate regression analysis |
| Measure of association | OR (table, one OR given for ABX exposure) |
| T0 | Asthma prevalence diagnosis/birth child (implicitly) |
| Confounders | Matched for age and gender; maternal history of asthma; vaginal bleeding during pregnancy; maternal age ≥ 30 ; exclusive breastfeeding (neonatally) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Current prevalence of asthma as a function of baseline (asthma prevalence diagnosis) exposure profile (maternal ABX use during pregnancy) in children aged 7-14 years adjusted for confounding by age (occurrence of asthma or inclusion as control, matching cases and control), gender, maternal history of asthma, vaginal bleeding during pregnancy, maternal age ≥ 30 and exclusive breastfeeding (neonatally).

Future prevalence of asthma as a function of baseline (at birth) exposure profile (maternal ABX use during pregnancy) in children aged 7-14 years adjusted for confounding by age (occurrence of asthma or inclusion as control, matching cases and control), gender, maternal history of asthma, vaginal bleeding during pregnancy, maternal age ≥ 30 and exclusive breastfeeding (neonatally).

12. Antibiotic use in early life, rural residence, and allergic diseases in Argentinean children.
Han et al.

| | |
|---|--|
| Number | 12 |
| Reference | Han et al. |
| Journal | J Allergy Clin Immunol Pract |
| YOP | 2017 |
| IF | 6.96 |
| Title | Antibiotic use in early life, rural residence, and allergic diseases in Argentinean children |
| Aim | <i>"...examine the relation between antibiotics use in early life and current asthma among children aged 6 to 7 years..."</i> |
| Domain | Children aged 6 to 7 years (title, introduction, methods & discussion) |
| Outcome | 'Current' asthma: parental report of physician diagnosed asthma and 'current' wheeze (in previous year) |
| Measure of frequency | / |
| Exposure | Any use of ABX in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Spanish ISAAC questionnaire distributed at school for parents of 6-7 year old children |
| "(Study) design"? | Yes (methods & discussion) |
| Data collection design | Cross-sectional study (abstract) |
| Data analysis design | Multivariate logistic regression Multivariable analysis |
| Measure of association | OR (methods, one odds ratio) |
| TO | At the end of the first year of life / 6-7 years of age (implicitly) |
| Confounders | Age (at inclusion in study); gender; parental history of allergy; paracetamol use first year of life; bronchiolitis first year of life; consumption of unpasteurized milk (first year of life) |
| Effect modifiers | Rural residence in the first year of life |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Current prevalence of 'current' asthma as a function of baseline (6-7 years of age) exposure profile (ABX use in the first year of life) in children aged 6-7 years adjusted for confounding by age (at inclusion in study), gender, parental history of allergy, paracetamol use (first year of life), bronchiolitis (first year of life), consumption of unpasteurized milk (first year of life) and effect modification by residence type (rural or urban) in the first year of life.

Future prevalence of 'current' asthma as a function of function of baseline (at the end of the first year of life) exposure profile (ABX use in the first year of life) in children aged 6-7 years adjusted for confounding by age (at inclusion in study), gender, parental history of allergy, paracetamol use (first year of life), bronchiolitis (first year of life), consumption of unpasteurized milk (first year of life) and effect modification by residence type (rural or urban) in the first year of life.

13. Hygiene factors associated with childhood food allergy and asthma. Gupta et al.

| | |
|--|--|
| Number | 13 |
| Reference | Gupta et al. |
| Journal | Allergy Asthma Proc |
| YOP | 2016 |
| IF | 2.6 |
| Title | Hygiene factors associated with childhood food allergy and asthma |
| Aim | <i>"...to assess whether hygiene factors are associated with a food allergy and/or asthma diagnosis. We investigated key hygiene factors, including ABX use, and their association with food allergy and asthma..."</i> |
| Domain | Children aged 0-21 years (abstract & methods) |
| Outcome | Asthma: physician diagnosis of asthma (0-21 years) (current) |
| Measure of frequency | Prevalence |
| Exposure | ABX use in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Questionnaire at the time of inclusion |
| "(Study) design"? | Yes (introduction) |
| Data collection design | Cross-sectional family-based study (abstract) |
| Data analysis design | Poisson regression model |
| Measure of association | Prevalence ratio's (per category of exposure, methods) |
| T0 | Inclusion in study (asthma occurrence, implicitly) |
| Confounders | parent reported infections (first year of life); eczema (overall); age (at inclusion in the study); household income (unspecified); number of siblings (current); child care (first 5 years of life); race; sex; pets (first year of life); parental atopy; breast feeding |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma as a function of baseline (at inclusion in study) exposure profile (ABX use in the first year of life) in children aged 0-21 years adjusted for confounding by parent reported infections (first year of life), eczema (overall), age (at inclusion in the study), household income (unspecified), number of siblings (current), child care (first 5 years of life), race, sex, pets (first year of life), parental atopy and breast feeding.

14. Antibiotic use during pregnancy and asthma in preschool children: the influence of confounding. Mulder et al.

| | |
|--|---|
| Number | 14 |
| Reference | Mulder et al. |
| Journal | Clinical & Experimental Allergy |
| YOP | 2016 |
| IF | 5.2 |
| Title | Antibiotic use during pregnancy and asthma in preschool children: the influence of confounding |
| Aim | <i>"...to assess the association between ABX use in pregnancy and the development of asthma in preschool children,... to evaluate the influence of confounding, results of the case-sibling analysis were compared with results obtained using a matched case-control design. In addition, we evaluated the influence of potential time trends in exposure frequencies in the case-sibling analysis."</i> |
| Domain | Preschool children up to the age of 5 years (introduction, methods & discussion) |
| Outcome | Asthma: at least 3 prescriptions for asthma medication within a 12 month period before the 5 th birthday |
| Measure of frequency | / |
| Exposure | Maternal exposure to ABX: at least 1 day supply of systemic ABX during pregnancy |
| Operationalization exposure | Dichotomous (Yes/No) Per trimester of exposure Per subgroup of ABX (5 classes) |
| Measurement exposure | Prescription database |
| "(Study) design"? | Yes (introduction, methods, results, discussion & appendix) |
| Data collection design | Case-sibling study (abstract, introduction & results) Nested case-sibling study (methods) Case-sibling analysis(discussion) Case-control study (abstract) Case-control analysis (results & discussion) Matched case-control design (introduction & methods) |
| Data analysis design | Conditional logistic regression |
| Measure of association | OR (for every exposure class, methods & results) |
| T0 | Birth child (implicitly) |
| Confounders | Gender; age at delivery; use of acid-suppressive drugs (during pregnancy); use of drugs indicated for allergic dermatitis (during pregnancy); use of drugs indicated for allergic rhinitis (during pregnancy); use of insulin (during pregnancy); potential time trends (in the case-sibling analysis); child birth order; use of asthma medication (during pregnancy); use of antidepressants (during pregnancy) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | Yes: publication |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma as a function of baseline (birth child) exposure profile (maternal exposure to ABX during pregnancy) in preschool children up to the age of 5 years

adjusted for confounding by gender, age at delivery, use of acid-suppressive drugs (during pregnancy), use of drugs indicated for allergic dermatitis (during pregnancy); use of drugs indicated for allergic rhinitis (during pregnancy), use of insulin (during pregnancy), child birth order, use of asthma medication (during pregnancy), use of antidepressants (during pregnancy) and potential time trends (in the case-sibling analysis only).

15. Relative importance and additive effects of maternal and infant risk factors on childhood asthma. Wu et al.

| | |
|--|---|
| Number | 15 |
| Reference | Wu et al. |
| Journal | Plos One |
| YOP | 2016 |
| IF | 2.8 |
| Title | Relative importance and additive effects of maternal and infant risk factors on childhood asthma |
| Aim | <i>"...to determine the relative impact and cumulative effect of in utero, perinatal and postnatal exposures that could be measured during pregnancy and infancy on the risk of developing early childhood asthma: maternal ABX use/urinary tract infection (UTI), mode of delivery, infant ABX use, and having older siblings. We also assessed the dose-dependent relationship of maternal ABX use/UTI, infant ABX use, and number of older siblings on the risk of developing early childhood asthma."</i> |
| Domain | Children aged 4.5 to 6 years (methods & results) |
| Outcome | Childhood asthma: ascertained between 4,5 and 6 years: ICD9 diagnosis or prescriptions for any short-acting β -agonist, 2 prescriptions for montelukast in a 365-day period, or a single prescription of any other asthma-specific medication |
| Measure of frequency | / |
| Exposure | ABX use during infancy (first 12 months) ABX use during pregnancy |
| Operationalization exposure | Number of courses of ABX (9 categories, from 0 to more than 8 doses for ABX use in infancy and 6 categories for ABX use during pregnancy) |
| Measurement exposure | Infant ABX use: medical claims prescription fill data Mothers: TennCare insurance |
| "(Study) design"? | No |
| Data collection design | Population-based birth cohort study (abstract, methods & discussion) |
| Data analysis design | Multivariable logistic regression model |
| Measure of association | OR (for every category OR, 0 courses as reference) |
| T0 | Age 1 / age 5 (implicitly) |
| Confounders | Maternal smoking during pregnancy; maternal asthma status; maternal age at delivery; maternal educational level; gestational age at delivery; infant's birth hospitalization length of stay; birth weight; infant's race; gender; having chronic lung disease (not specified); having congenital heart disease (not specified); type of most severe bronchiolitis healthcare encounters experienced during infancy; birth year; study site |
| Effect modifiers | Subgroup analysis: birth weight, KPNC (Kaiser Permanente Northern California) or TennCare (Tennessee Medicaid program) |
| Justification selection confounders/effect modifiers? | Yes: covariates chosen a priori based on clinical relevance |
| Reporting guideline or theoretical work? | / |

Theoretical design: 2 possibilities

Future prevalence of asthma as a function of baseline (age 1) exposure profile (ABX use during the first 12 months of life / maternal ABX use during pregnancy) in children aged 4.5 to 6 years adjusted for confounding by maternal smoking during pregnancy, maternal asthma

status, maternal age at delivery, maternal educational level, gestational age at delivery, infant's birth hospitalization length of stay, birth weight, infant's race, gender, having chronic lung disease (not specified), having congenital heart disease (not specified), type of most severe bronchiolitis healthcare encounters experienced during infancy, birth year, study site and effect modification by birth weight.

Current prevalence of asthma as a function of baseline (age 5) exposure profile (ABX use in the first 12 months of life / maternal ABX use during pregnancy) in children aged 4.5 to 6 years adjusted for confounding by maternal smoking during pregnancy, maternal asthma status, maternal age at delivery, maternal educational level, gestational age at delivery, infant's birth hospitalization length of stay, birth weight, infant's race, gender, having chronic lung disease (not specified), having congenital heart disease (not specified), type of most severe bronchiolitis healthcare encounters experienced during infancy, birth year, study site and effect modification by birth weight.

**16. Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children.
Korpela et al.**

| | |
|--|--|
| Number | 16 |
| Reference | Korpela et al. |
| Journal | Nature Communications |
| YOP | 2016 |
| IF | 12.1 |
| Title | Intestinal microbiome is related to lifetime antibiotic use in Finnish pre-school children |
| Aim | <i>"...to investigate the short- and long-term effects of ABX on preschool children's intestinal microbiome and health."</i> |
| Domain | Children aged 2-7 years (title, introduction, results & methods) |
| Outcome | Diagnosed asthma: current or developing asthma (age 2-7 years) |
| Measure of frequency | / |
| Exposure | Overall lifetime ABX use: macrolide use during the first 2 years of life |
| Operationalization exposure | Dichotomous (more than 2 courses of macrolides in the first 2 years of life vs. non-exposed) |
| Measurement exposure | National database on prescription drug purchase |
| "(Study) design"? | No |
| Data collection design | Cohort (introduction, results, discussion & methods) |
| Data analysis design | Fisher's test |
| Measure of association | OR for the group that used more than 2 courses of macrolides in the first two years of life |
| T0 | Asthma diagnosis / at 2 years of age (implicitly) |
| Confounders | / |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Current prevalence of asthma as a function of baseline (asthma diagnosis) exposure status (macrolide use during the first 2 years of life) in children aged 2-7 years.

Future prevalence of asthma as a function of baseline (at 2 years of age) exposure profile (macrolide use during the first 2 years of life) in children aged 2-7 years.

17. Periconceptual and gestational exposure to antibiotics and childhood asthma. Chu et al.

| | |
|---|---|
| Number | 17 |
| Reference | Chu et al. |
| Journal | Plos One |
| YOP | 2015 |
| IF | 3.0 |
| Title | Periconceptual and gestational exposure to antibiotics and childhood asthma |
| Aim | <i>"...to assess the associations between maternal exposure to different types of ABX before and during pregnancy and childhood asthma..."</i> |
| Domain | Children up to the age of 7 years (introduction & methods) |
| Outcome | Definite asthma by 7 years of age: medical records |
| Measure of frequency | Prevalence |
| Exposure | Maternal ABX exposure: ABX by oral or injection during 4 weeks prior to last menstrual period or at any month during pregnancy |
| Operationalization exposure | 6 categories of ABX subdivided in 5 categories for timing of exposure (total exposure, 4 week before last menstrual period, 1 st trimester, 2 nd trimester and 3 rd trimester) |
| Measurement exposure | Questionnaires during pregnancy |
| "(Study) design"? | No |
| Data collection design | Prospective cohort study? (discussion) |
| Data analysis design | Multilevel multiple logistic regression |
| Measure of association | OR (per category of exposure, methods) |
| T0 | Birth child / 7 years of age (implicitly) |
| Confounders | maternal age at delivery; race (mother); number of previous births; smoking during pregnancy; maternal drug allergy history; married at pregnancy; educational level; maternal asthma history |
| Effect modifiers | stratification by time of medication (not explicitly) |
| Justification selection confounders/effect modifiers? | Yes: previous publication |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Future prevalence of asthma as a function of baseline (birth child) exposure profile (**maternal exposure to ABX 4 weeks prior to the last menstrual period or at any time during pregnancy**) in **children up to the age of 7 years** adjusted for confounding by maternal age at delivery, race (mother), number of previous births, smoking during pregnancy, maternal drug allergy history, married at pregnancy, educational level, maternal asthma history (and effect modification by timing of medication?).

Current prevalence of asthma as a function of baseline (at 7 years of age) exposure profile (**maternal exposure to ABX 4 weeks prior to the last menstrual period or at any time during pregnancy**) in **children up to the age of 7 years** adjusted for confounding by **maternal age at delivery, race (mother), number of previous births, smoking during pregnancy, maternal drug allergy history, married at pregnancy, educational level, maternal asthma history (and effect modification by timing of medication?)**.

18. Antibiotic exposure in the first year of life and later treated asthma, a population based birth cohort study of 143000 children. Pitter et al.

| | |
|--|--|
| Number | 18 |
| Reference | Pitter et al. |
| Journal | Eur J Epidemiol |
| YOP | 2015 |
| IF | 7.1 |
| Title | Antibiotic exposure in the first year of life and later treated asthma, a population based birth cohort study of 143000 children |
| Aim | <i>"...to evaluate whether exposure to ABX during the first 12 months of life increases the risk of subsequent treated asthma..."</i> |
| Domain | Children up to the age of 17 years (title, introduction, methods, results & discussion) |
| Outcome | Treated asthma: at least 2 prescriptions at different time points within a 12 months period, of anti-asthmatic drugs 'Current' asthma at age 6 years or older and at age 13 years or older |
| Measure of frequency | Incidence rate ratio |
| Exposure | ABX exposure during the first 12 months of life: prescription of at least 1 antibiotic |
| Operationalization exposure | Dichotomous, ABX ever (Yes/No) Number of courses (4 categories) Penicillins (Yes/No) Cephalosporins (Yes/No) Macrolides (Yes/No) Other drugs (Yes/No) |
| Measurement exposure | Drug prescription records |
| "(Study) design"? | Yes (discussion & introduction) |
| Data collection design | Population-based birth cohort study (abstract & discussion) |
| Data analysis design | Poisson models |
| Measure of association | Incidence rate ratio's (for every category, methods) |
| T0 | At 13 months of age (explicitly) |
| Confounders | year of birth; maternal age at birth; gestational age; type of delivery; sex; mother's formal education; birth weight; RTI requiring hospital admission during the first 12 months of life (confounding by indication) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset/'current' asthma onset at age 6 years or older/'current' asthma onset at age 13 years or older as a function of baseline (at 13 months of age) exposure profile (ABX use during the first 12 months of life) in children up to the age of 17 years adjusted for confounding by year of birth, maternal age at birth, gestational age, type of delivery, sex, mother's formal education, birth weight, RTI requiring hospital admission during the first 12 months of life (confounding by indication).

19. Association between antibiotic exposure, bronchiolitis, and TLR4 (rs1927911) polymorphisms in childhood asthma. Lee et al.

| | |
|--|---|
| Number | 19 |
| Reference | Lee et al. |
| Journal | Allergy Asthma Immunol Res |
| YOP | 2015 |
| IF | 2.3 |
| Title | Association between antibiotic exposure, bronchiolitis, and TLR4 (rs1927911) polymorphisms in childhood asthma |
| Aim | <i>"...investigate the risk factors involved in the development of asthma during early life and their interactions. Specifically, we investigated whether ABX exposure in the first year of life and a history of physician diagnosed bronchiolitis in the first 2 years of life were associated with an increased risk of childhood asthma. In addition, we evaluated whether a polymorphism in TLR4 (rs1927911) modulates the impact of these environmental factors..."</i> |
| Domain | Children (methods, results & discussion) |
| Outcome | Prevalence of asthma: ever been diagnosed with asthma |
| Measure of frequency | Prevalence |
| Exposure | ABX exposure in the first year of life |
| Operationalization exposure | Dichotomous (Yes/no) |
| Measurement exposure | Modified version of the ISAAC questionnaire |
| "(Study) design"? | No |
| Data collection design | Cross-sectional study (abstract & discussion) |
| Data analysis design | Logistic regression |
| Measure of association | OR (OR for ABX exposure category yes vs. no, methods) |
| T0 | Inclusion in study (implicitly) |
| Confounders | Age (at inclusion); BMI (at inclusion); household income (at inclusion); parental history of allergic disease; sex; school area; ETS (at inclusion) |
| Effect modifiers | stratification by genotype TLR4: modifies combined effect of infant ABX exposure in the first year of life and history of physician diagnosed bronchiolitis in the first 2 years of life on the development of asthma |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma as a function of baseline (inclusion in study) exposure profile (**ABX use in the first year of life**) in **children** adjusted for confounding by age (at inclusion), BMI (at inclusion), household income (at inclusion), parental history of allergic disease, sex, school area, ETS (at inclusion) and effect modification by genotype TLR4.

20. The relationship between prenatal antibiotic use and asthma in at-risk children. Lapin et al.

| | |
|--|---|
| Number | 20 |
| Reference | Lapin et al. |
| Journal | Ann Allergy Asthma Immunol |
| YOP | 2015 |
| IF | 3.4 |
| Title | The relationship between prenatal antibiotic use and asthma in at-risk children |
| Aim | <i>"...we investigated the effects of prenatal ABX use with the subsequent development of asthma by year 3 and wheezing in the third year..."</i> |
| Domain | At-risk children up to the age of 3 years (title & discussion) |
| Outcome | Asthma: Asthma diagnosis by year 3 (ever having asthma) (diagnosis by a physician, parent-reported) |
| Measure of frequency | Incidence |
| Exposure | Systemic ABX us: antibiotic use during pregnancy |
| Operationalization exposure | Prenatal ABX use: dichotomous (yes/no) (any ABX during pregnancy) Timing of ABX use (first trimester vs. second and third trimester) |
| Measurement exposure | Questionnaires |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Cohort (discussion) Prospective study (Introduction) |
| Data analysis design | Multivariable logistic regression |
| Measure of association | OR (results, per category) |
| T0 | At 1 year of age (implicitly) |
| Confounders | Study intervention; maternal history of asthma; maternal ethnicity (Mexican ancestry); ibuprofen use during pregnancy; maternal age; smoking during pregnancy; exposure to smoke in the home in the first year of life; child antibiotic use for respiratory reasons; vitamin use of the mother during pregnancy; any ibuprofen use during the child's first year of life; any respiratory infections during the child's first year of life |
| Effect modifiers | Vitamin use of the mother during pregnancy; maternal history of asthma; any ibuprofen use of the child in the first year of life; children who did not use ABX in the first year of life; respiratory infections in the child's first year of life; smoking in the home during the child's first year of life |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset as a function of baseline (1 year of age) exposure profile (**maternal ABX use during pregnancy**) in **children up to the age of 3 years** adjusted for confounding by study intervention, maternal history of asthma, maternal ethnicity (Mexican ancestry), ibuprofen use during pregnancy, maternal age, smoking during pregnancy, exposure to smoke in the home in the first year of life, child antibiotic use for respiratory reasons, vitamin use of the mother during pregnancy, any ibuprofen use during the child's first year of life, any respiratory infections during the child's first year of life and effect modification by vitamin use of the mother during pregnancy, maternal history of asthma, any ibuprofen use of the child in the first year of life, children who did not use ABX in the first year of life, respiratory infections in the child's first year of life and smoking in the home during the child's first year of life.

45. Antibiotic use in infancy and symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 and 7 years old: International study of asthma and allergies in childhood phase III. Foliaki et al.

| | |
|--|---|
| Number | 45 |
| Reference | Foliaki et al. |
| Journal | J Allergy Clin Immunol |
| YOP | 2009 |
| IF | 9.1 |
| Title | Antibiotic use in infancy and symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 and 7 years old: International study of asthma and allergies in childhood phase III |
| Aim | <i>"...to study the associations between parental-reported ABX use in the first year of life and current symptoms of asthma, rhinoconjunctivitis, and eczema in children 6 and 7 years old..."</i> |
| Domain | Children aged 6-7 years (title, introduction, methods, results & discussion) |
| Outcome | Severe asthma symptoms: ('current') wheezing causing sleep disturbance, or wheezing limiting speech, or at least 4 attacks of wheezing in the past 12 months Asthma ever |
| Measure of frequency | / |
| Exposure | ABX use in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | ISAAC questionnaire |
| "(Study) design"? | No |
| Data collection design | Cross-sectional study (discussion) |
| Data analysis design | Generalized linear mixed models Multiple regression analysis |
| Measure of association | Prevalence odds ratio's (methods, one OR for asthma) |
| T0 | 6-7 years of age (implicitly) |
| Confounders | Sex; language; maternal education; ever breast fed; current diet (at 6-7 years of age); region (not specified); gross national income (not specified); paracetamol use first year of life; parental smoking (not specified); siblings (not specified) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma at as a function of baseline (6-7 years if age) exposure profile (**ABX use in the first year of life**) in **6 to 7 year old children** adjusted for confounding by sex, language, ever breast fed (first year of life), paracetamol use (first year of life), maternal education, region (not specified), gross national income (not specified); parental smoking (not specified), siblings (not specified) and current diet (at 6-7 years of age).

46. Cross-sectional survey of risk factors for asthma in 6-7 year-old children in New Zealand: International study of asthma and allergies in childhood phase three. Mitchell et al.

| | |
|--|--|
| Number | 46 |
| Reference | Mitchell et al. |
| Journal | Journal of Pediatrics and Child Health |
| YOP | 2009 |
| IF | 1.1 |
| Title | Cross-sectional survey of risk factors for asthma in 6-7 year-old children in New Zealand: International study of asthma and allergies in childhood phase three |
| Aim | <i>"...to identify and quantify risk factors for asthma in over 10000 6-7-year-old children..."</i> |
| Domain | Children aged 6-7 years (title, introduction, methods, results & discussion) |
| Outcome | Wheeze in the last 12 months (6-7 years, 'current' wheeze) |
| Measure of frequency | Prevalence |
| Exposure | ABX in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | ISAAC questionnaire at 6-7 years |
| "(Study) design"? | No |
| Data collection design | Cross-sectional survey (abstract & discussion) |
| Data analysis design | Logistic regression |
| Measure of association | OR (results, 1 OR for asthma) |
| TO | 6-7 years of age (implicitly) |
| Confounders | Gender; school decile (at 6-7 years of age); maternal farm animal exposure during pregnancy; born in New Zealand; number of older siblings (at 6-7 years of age); number of younger siblings (at 6-7 years of age); contact farm animals in first year; paracetamol use in first year; current paternal and maternal smoking (at 6-7 years of age); cooking appliance (at 6-7 years of age); television viewing (at 6-7 years of age); ethnicity; maternal education (at 6-7 years of age); breast feeding (first year of life); maternal smoking first year; cat at home in the first year; dog at home in the first year; food intake (at 6-7 years of age); truck passage street (at 6-7 years of age); physical activity (at 6-7 years of age) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of wheeze as a function of baseline (6-7 years of age) exposure profile (**ABX use in the first year of life**) in **children aged 6-7 years** adjusted for confounding by gender, ethnicity, maternal farm animal exposure (during pregnancy), born in New Zealand, contact farm animals (first year of life), paracetamol use (first year of life), breast feeding (first year of life), maternal smoking (first year of life), cat at home (first year of life), dog at home (first year of life), school decile (at 6-7 years of age), number of older siblings (at 6-7 years of age), number of younger siblings (at 6-7 years of age), current paternal and maternal smoking (at 6-7 years of age), cooking appliance (at 6-7 years of age), television viewing (at 6-

7 years of age), maternal education (at 6-7 years of age), food intake (at 6-7 years of age), truck passage street (at 6-7 years of age) and physical activity (at 6-7 years of age).

47. Antibiotic use in children is associated with increased risk of asthma. Marra et al.

| | |
|--|---|
| Number | 47 |
| Reference | Marra et al. |
| Journal | Pediatrics |
| YOP | 2009 |
| IF | 4.6 |
| Title | Antibiotic use in children is associated with increased risk of asthma |
| Aim | <i>"...to explore the association between exposure to ABX in the first year of life and the subsequent development of asthma... Specifically we sought to evaluate the association between antibiotics prescribed within the first year of life and the development of asthma, and to evaluate a potential dose-response relationship between the number of courses of antibiotics received and the development of asthma."</i> |
| Domain | Children (title, introduction, results & discussion) |
| Outcome | Asthma diagnosis: hospital discharge for asthma or 2 medical fee-for-service claims within a moving 12-months period or 2 prescriptions for a known asthma medication within a moving 12-months period |
| Measure of frequency | Incidence |
| Exposure | Exposure to ABX in the first year of life |
| Operationalization exposure | Dichotomous (Ever/Never) Number of ABX prescriptions (4 levels) Type of antibiotic dispensed (6 categories) |
| Measurement exposure | Administrative health data (database) |
| "(Study) design"? | Yes (discussion) |
| Data collection design | Longitudinal cohort study (methods) Observational prospective cohort study (discussion) |
| Data analysis design | Cox proportional hazard |
| Measure of association | HR Incidence rate asthma (methods, HR for development of asthma for every category of exposure) |
| T0 | At 1 year of age (implicitly) |
| Confounders | Gender; SES at birth; urban or rural address at birth; birth weight; gestational age; delivery method; frequency of physician visits (first year of life); allergist/respirologist/immunologist visit (first year of life); hospital visit involving surgery (first year of life); congenital anomalies (first year of life); related diseases (otitis media/bronchitis/URTI and LRTI; first year of life) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future incidence of asthma onset as a function of baseline (at 1 year of age) exposure profile (**ABX use in the first year of life**) in **children** adjusted for confounding by gender, birth weight, gestational age, delivery method, SES at birth, urban or rural address at birth, frequency of physician visits (first year of life), allergist/respirologist/immunologist visit (first year of life), hospital visit involving surgery (first year of life), congenital anomalies (first year of life) and related diseases (otitis media; bronchitis; URTI and LRTI) (first year of life).

48. Antibiotic use in the first year of life and risk of atopic disease in early childhood. Kusel et al.

| | |
|--|--|
| Number | 48 |
| Reference | Kusel et al. |
| Journal | Clinical and Experimental Allergy |
| YOP | 2008 |
| IF | 3.6 |
| Title | Antibiotic use in the first year of life and risk of atopic disease in early childhood |
| Aim | <i>"...to investigate the association between ABX use in the first year of life and the development of atopic disease at 5 years."</i> |
| Domain | Preschool children at high risk for atopy (introduction, methods & discussion) |
| Outcome | 'Current' asthma: doctor's diagnosis of asthma & 'current' wheeze between 4-5 years of age Atopic 'current' asthma: 'current' asthma + positive SPT at 5 years or elevated serum total IgE at 5 years |
| Measure of frequency | / |
| Exposure | ABX use in the first year of life |
| Operationalization exposure | Categorical (ABX use 0-6 months, 7-12 months and 1-12 months) |
| Measurement exposure | Daily diary |
| "(Study) design"? | No |
| Data collection design | High-risk birth cohort (introduction & discussion) Prospective birth cohort (abstract) |
| Data analysis design | Propensity score adjustment Logistic regression |
| Measure of association | OR (results, OR for asthma for every category of ABX exposure) |
| T0 | At 1 year of age (implicitly) |
| Confounders | Propensity score (antibiotic predictor group); number of doctor's visits; sex; childcare (first year of life); pets (first year of life) |
| Effect modifiers | Number of doctor's visits (first year of life); sex; childcare (first year of life); pets (first year of life); ABX use between 0-6 months |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Future prevalence of 'current' asthma/atopic 'current' asthma as a function of baseline (at 1 year of age) exposure profile (ABX use in the first year of life) in preschool children at high risk for atopy adjusted for confounding by propensity score (antibiotics predictor group), sex, childcare (first year of life), pets (first year of life), number of doctor's visits (unspecified)) and effect modification by sex, ABX use (between 0-6 months of age), childcare (first year of life), pets (first year of life) and number of doctor's visits (unspecified).

49. Determinants of the incidence of childhood asthma: a two-stage case-control study. Martel et al.

| | |
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| Number | 49 |
| Reference | Martel et al. |
| Journal | Am J Epidemiol |
| YOP | 2008 |
| IF | 5.4 |
| Title | Determinants of the incidence of childhood asthma: a two-stage case-control study |
| Aim | <i>"... identifying the independent effects of 47 potential predictors, measured during pregnancy and after birth, on the incidence of asthma development in children within the first 10 years of life."</i> |
| Domain | Children up to the age of 10 years (introduction, methods, results & discussion) |
| Outcome | Childhood asthma: at least 1 diagnosis of asthma and at least 1 prescription for asthma medication within a 2-year period |
| Measure of frequency | Incidence |
| Exposure | Mean number of ABX prescriptions filled per month during pregnancy ABX in the first 6 months of life or ABX prior to index date |
| Operationalization exposure | Dichotomous for ABX use child (Yes/No) Not clear how they coded the variable for the mother |
| Measurement exposure | From administrative linked health databases |
| "(Study) design"? | Yes (methods) |
| Data collection design | Case-control study, nested in a cohort of children (methods) Two-stage case-control study (title, abstract & methods) |
| Data analysis design | Conditional logistic regression |
| Measure of association | Rate ratio's (methods, 1 rate ratio for ABX exposure in child, 1 rate ratio for ABX exposure in pregnancy, RR per additional prescription) OR (idem) |
| T0 | First occurrence of an asthma diagnosis (code) and a filled prescription for asthma medication within a 2 year period: refer to this as index date (explicitly) |
| Confounders | Age at diagnosis; gender; allergic disease prior to index date; administration of oxygen to newborn in hospital; one or more diagnoses of bronchopulmonary disease (prior to index date); maternal receipt of social welfare (in year before or during pregnancy); intranasal corticosteroids during pregnancy; paternal history of asthma; presence of wood-burning fireplace in home (prior to index date); day-care attendance (prior to index date); pets in the home (for more than 2 months) (prior to index date); breast feeding; asthma during pregnancy; asthma siblings (prior to index date) |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current incidence of asthma as a function of baseline (first occurrence of an asthma diagnosis (code) and a filled prescription for asthma medication within a 2 year period) exposure profile (maternal exposure to ABX prescriptions filled during pregnancy/ ABX use in

the first 6 months of life or prior to index date) in children up to the age of 10 years adjusted for confounding by gender, intranasal corticosteroids during pregnancy, asthma during pregnancy, administration of oxygen to newborn in hospital, age at diagnosis, allergic disease prior to index date, presence of wood-burning fireplace in home prior to index date, day-care attendance prior to index date, pets in home (for more than 2 months) prior to index date, asthma siblings (prior to index date), one or more diagnoses of bronchopulmonary disease (prior to index date); maternal receipt of social welfare (in year before or during pregnancy), paternal history of asthma (prior to index date) and breast feeding.

50. The association of early life exposure to antibiotics and the development of asthma, eczema and atopy in a birth cohort: confounding or causality? Wickens et al.

| | |
|--|---|
| Number | 50 |
| Reference | Wickens et al. |
| Journal | Clinical and Experimental Allergy |
| YOP | 2008 |
| IF | 3.6 |
| Title | The association of early life exposure to antibiotics and the development of asthma, eczema and atopy in a birth cohort: confounding or causality? |
| Aim | <i>"...to investigate the relationship between ABX and the subsequent development of asthma, eczema and atopy... A secondary aim was to determine whether this association is due to confounding by chest infections in infancy."</i> |
| Domain | Children (introduction & methods) |
| Outcome | 'Current' asthma: asthma + wheeze and/or inhaler use occurring in the previous 12 months |
| Measure of frequency | Prevalence |
| Exposure | ABX use: ever in the first 3 months ABX use: between 3 and 15 months |
| Operationalization exposure | 3 categories: systemic ABX use, 1 chest infections, 2+ chest infection for 3 months, 15 months and 4 years |
| Measurement exposure | Questionnaire at 3 and 15 months of age |
| "(Study) design"? | No |
| Data collection design | Prospective study (discussion) Birth cohort study (abstract) Cohort (discussion) |
| Data analysis design | Cross-sectional associations Multivariate logistic regression |
| Measure of association | OR (results, OR for both outcomes per category of exposure) |
| T0 | Asthma diagnosis period (implicitly) |
| Confounders | Number of chest infections (0-4 years of age); gender; prioritized ethnicity; family history of asthma, eczema/hay fever; ABX use during outcome period; household smoking (any by father or mother); ear infection (0-4 years of age); parity (before 3 months of age) |
| Effect modifiers | Number of chest infections (0-4 years of age) |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of 'current' asthma (between 0-15 months of age/between 3-4 years of age) as a function of baseline (asthma diagnosis period) exposure profile (ABX use before 3 months of age/ABX use between 3-15 months of age/ ABX use before 4 years of age) in children adjusted for confounding by gender, prioritized ethnicity (before 3 months of age), parity (before 3 months of age), ABX use during outcome period, number of chest infections (0-4 years of age), ear infection (0-4 years of age), family history of asthma, eczema or hay fever (family history), household smoking (any by father or mother) and effect modification by number of chest infections (0-4 years of age).

51. Risk factors for asthma at 3.5 and 7 years of age. Mitchell et al.

| | |
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| Number | 51 |
| Reference | Mitchell et al. |
| Journal | Clinical and Experimental Allergy |
| YOP | 2007 |
| IF | 3.7 |
| Title | Risk factors for asthma at 3.5 and 7 years of age |
| Aim | <i>"...to examine risk factors for asthma in children aged 3.5 and 7 years of age, with particular emphasis on environmental exposures in infancy including birth weight, maternal smoking, breast feeding, day care, ABX treatment and exposure to inhaled allergens."</i> |
| Domain | Children aged 3.5 and 7 years of age (introduction, methods, results & discussion) |
| Outcome | 'Current' wheeze (past 12 months): asthma at 3.5 and 7 years of age |
| Measure of frequency | Prevalence |
| Exposure | ABX in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | Questionnaire at 3.5 years of age |
| "(Study) design"? | Yes (methods & discussion) |
| Data collection design | Prospective study (discussion) |
| Data analysis design | Generalized linear models Logistic regression |
| Measure of association | OR (methods, OR for exposure yes vs. no) |
| T0 | At 1 year of age / asthma onset (at 3.5 or 7 years of age) (implicitly) |
| Confounders | Age (at inclusion); smoking (pregnancy); day care or looked after by others (first year of life); presence of dog (first year of life); used pillow (first year of life); used quilt (first year of life); slept on used mattress (first year of life); hospitalized (first year of life); asthma in parents (current); maternal smoking (current); eczema in child (current); rhinitis in child (current); positive skin test in child (current); gender; SGA (at birth); first born (at birth); SES (at birth); damp patches on walls in winter (first year of life); fungus/mould all year (first year of life); presence of cat (first year of life); presence of bird (first year of life); slept on sheepskin (first year of life); children in household (at 1 year); duration of breast feeding (first year of life); carpet in bedroom (first year of life); trucks passing house frequently (7 years of age) |
| Effect modifiers | Interaction with age (at inclusion) and significant factors: presence of dog (first year of life); maternal smoking during pregnancy; used quilt (first year of life); slept on used mattress (first year of life); hospitalization (first year of life); parental asthma; eczema in child (current); rhinitis in child (current); positive skin test in child (current); current maternal smoking; day care or looked after by others (first year of life) |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Future prevalence of 'current' wheeze as a function of as a function of baseline (at 1 year of age) exposure profile (ABX use in the first year of life) in children aged 3.5 and 7 years of age

for confounding by age (at inclusion), smoking (pregnancy), day care or looked after by others (first year of life), presence of dog (first year of life), used pillow (first year of life), used quilt (first year of life), slept on used mattress (first year of life), hospitalized (first year of life), asthma in parents (current), maternal smoking (current), eczema in child (current), rhinitis in child (current), positive skin test in child (current), gender, SGA (at birth), first born (at birth), SES (at birth), damp patches on walls in winter (first year of life), fungus/mould all year (first year of life), presence of cat (first year of life), presence of bird (first year of life), slept on sheepskin (first year of life), children in household (at 1 year), duration of breast feeding (first year of life), carpet in bedroom (first year of life), trucks passing house frequently (7 years of age) and effect modification by age, presence of dog (first year of life), maternal smoking during pregnancy, used quilt (first year of life), slept on used mattress (first year of life), hospitalization (first year of life), parental asthma, eczema in child (current), rhinitis in child (current), positive skin test in child (current), current maternal smoking and day care or looked after by others (first year of life).

Current prevalence of 'current' wheeze as a function of baseline (asthma onset at 3.5 or 7 years of age) exposure profile (ABX use in the first year of life) in children aged 3.5 and 7 years of age adjusted for confounding by age (at inclusion), smoking (pregnancy), day care or looked after by others (first year of life), presence of dog (first year of life), used pillow (first year of life), used quilt (first year of life), slept on used mattress (first year of life), hospitalized (first year of life), asthma in parents (current), maternal smoking (current), eczema in child (current), rhinitis in child (current), positive skin test in child (current), gender, SGA (at birth), first born (at birth), SES (at birth), damp patches on walls in winter (first year of life), fungus/mould all year (first year of life), presence of cat (first year of life), presence of bird (first year of life), slept on sheepskin (first year of life), children in household (at 1 year), duration of breast feeding (first year of life), carpet in bedroom (first year of life), trucks passing house frequently (7 years of age) and effect modification by age, presence of dog (first year of life), maternal smoking during pregnancy, used quilt (first year of life), slept on used mattress (first year of life), hospitalization (first year of life), parental asthma, eczema in child (current), rhinitis in child (current), positive skin test in child (current), current maternal smoking and day care or looked after by others (first year of life).

52. Increased risk of childhood asthma from antibiotics use in early life. Kozyrskyj et al.

| | |
|---|---|
| Number | 52 |
| Reference | Kozyrskyj et al. |
| Journal | Chest |
| YOP | 2007 |
| IF | 4.1 |
| Title | Increased risk of childhood asthma from antibiotics use in early life |
| Aim | <i>"...examine the association between oral ABX use in the first year of life and asthma at age 7 years..."</i> |
| Domain | Children 7 years of age (introduction, methods, results & discussion) |
| Outcome | 'Current' asthma at age 7: at least 2 physician visits for asthma, 1 asthma hospitalization or 2 prescriptions for any asthma drug in the year following the 7 th birthday |
| Measure of frequency | Prevalence |
| Exposure | ABX use during the first year of life (number of oral ABX prescriptions) |
| Operationalization exposure | Number of oral ABX prescriptions (4 categories) |
| Measurement exposure | Health-care administrative data |
| "(Study) design"? | Yes (introduction) |
| Data collection design | Longitudinal study (abstract & methods) Cohort (discussion) |
| Data analysis design | Multivariate logistic regression |
| Measure of association | OR (results, for each category of exposure OR for outcome) |
| T0 | At 1 year of age / at 7 years of age (implicitly) |
| Confounders | Gender; maternal history of asthma; number of health care visits (first year of life); number of non-respiratory tract infections (unspecified); number of siblings (at 7 years of age); urban/rural location (unspecified); number of LRTI (unspecified); household income (unspecified) |
| Effect modifiers | Maternal history of asthma; presence or absence of dog during birth year (during birth year); urban/rural location (unspecified) |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Future prevalence of 'current' asthma as a function of baseline (at 1 year of age) exposure profile (**ABX use in the first year of life**) in **children 7 years of age** adjusted for confounding by gender, maternal history of asthma, number of non-respiratory tract infections (unspecified), urban/rural location (unspecified), household income (unspecified), number of LRTI (unspecified), number of health care visits (first year of life), number of siblings (at 7 years of age) and effect modification by maternal history of asthma, urban/rural location (unspecified) and presence or absence of dog (during birth year).

Current prevalence of 'current' asthma as a function of baseline (at 7 years of age) exposure profile (**ABX use in the first year of life**) in **children 7 years of age** adjusted for confounding by gender, maternal history of asthma, number of non-respiratory tract infections (unspecified), urban/rural location (unspecified), household income (unspecified), number of LRTI (unspecified), number of health care visits (first year of life), number of siblings (at 7 years of age) and effect modification by maternal history of

asthma, urban/rural location (unspecified) and presence or absence of dog (during birth year).

53. Identification of asthma risk factors in Mexico City in an International Study of Asthma and Allergy in Childhood survey. Del-Rio-Navarro et al.

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| Number | 53 |
| Reference | Del-Rio-Navarro et al. |
| Journal | Allergy and Asthma Proceedings |
| YOP | 2006 |
| IF | 0.75 |
| Title | Identification of asthma risk factors in Mexico City in an International Study of Asthma and Allergy in Childhood survey |
| Aim | <i>"...perform a risk analysis based on the ISAAC survey in Mexico."</i> |
| Domain | Childhood (6-7 years of age and 13-14 years of age) (methods, results & discussion) |
| Outcome | Cumulative prevalence of asthma (wheezing ever) Current prevalence of asthma (wheezing last 12 months) |
| Measure of frequency | Cumulative prevalence Current prevalence |
| Exposure | ABX use in the first year of life |
| Operationalization exposure | Dichotomous (Yes/No) |
| Measurement exposure | ISAAC questionnaire at age 6-7 years old |
| "(Study) design"? | No |
| Data collection design | Cross-sectional survey (methods) |
| Data analysis design | Logistic regression using the forward conditional method |
| Measure of association | OR (one OR for exposure related to asthma, results) |
| T0 | 6-7 years of age and 13-14 years of age (implicitly) |
| Confounders | / |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | No |
| Reporting guideline or theoretical work? | No |

Theoretical design:

Current prevalence of asthma/cumulative prevalence of asthma as a function of baseline (6-7 years of age/13-14 years of age) exposure profile (ABX use in the first year of life) in children aged 6-7 years of age and 13-14 years of age.

54. Allergic disease and sensitization in Steiner school children. Floïstrup et al.

| | |
|---|--|
| Number | 54 |
| Reference | Floïstrup et al. |
| Journal | J Allergy Clin Immunol |
| YOP | 2005 |
| IF | 7.7 |
| Title | Allergic disease and sensitization in Steiner school children |
| Aim | <i>"...to identify possible protective factors for allergy associated with the anthroposophic lifestyle.."</i> |
| Domain | Children aged 5 to 13 years (title, introduction, methods, results & discussion) |
| Outcome | Doctor's diagnosis of asthma: ever asthma diagnosis |
| Measure of frequency | Prevalence |
| Exposure | Use of ABX in the first year of life |
| Operationalization exposure | Never/first use after 12 months of age and first use first 12 months of age |
| Measurement exposure | Parental questionnaire among children age 5-13 years |
| "(Study) design"? | Yes (discussion & methods) |
| Data collection design | Cross-sectional (abstract, methods & discussion) |
| Data analysis design | Logistic regression |
| Measure of association | OR (methods, for every category of ABX exposure) |
| T0 | 5-13 years of age / 1 year of age (implicitly) |
| Confounders | Age (at inclusion in the study); sex; country; maternal smoking during pregnancy; maternal asthma and/or rhinoconjunctivis; paternal asthma and/or rhinoconjunctivis; having household pets during the first year of life; use of antipyretics during the first year of life; measles infection (not specified); type of diet (not specified); MMR vaccination; current smoking in the household; older siblings; parental education |
| Effect modifiers | / |
| Justification selection confounders/effect modifiers? | Yes: referral to previous results in other publication |
| Reporting guideline or theoretical work? | No |

Theoretical design: 2 possibilities

Current prevalence of asthma as a function of baseline (at 5-13 years of age) exposure profile (ABX use in the first year of life) in children aged 5-13 years of age adjusted for confounding by age (at inclusion in the study), sex, country, maternal smoking during pregnancy, maternal asthma and/or rhinoconjunctivis, paternal asthma and/or rhinoconjunctivis, having household pets during the first year of life, use of antipyretics during the first year of life, measles infection (not specified), type of diet (not specified), MMR vaccination, current smoking in the household, older siblings and parental education.

Future prevalence of asthma as a function of baseline (at 1 year of age) exposure profile (ABX use in the first year of life) in children aged 5-13 years of age adjusted for confounding by age (at inclusion in the study), sex, country, maternal smoking during pregnancy, maternal asthma and/or rhinoconjunctivis, paternal asthma and/or rhinoconjunctivis, having household pets during the first year of life, use of antipyretics during the first year of life, measles infection (not specified), type of diet (not specified), MMR vaccination, current smoking in the household, older siblings and parental education.