**ASTHMA PHENOTYPE ALGORITHM**

**Background:**

Asthma is [chronic](http://en.wikipedia.org/wiki/Chronic_%28medicine%29) inflammatory [disease](http://en.wikipedia.org/wiki/Disease) of the [airways](http://en.wikipedia.org/wiki/Bronchi) characterized by airway inflammation, reversible airflow obstruction and bronchial hyperresponsiveness. It is a complex disease caused by environmental and genetic factors. An estimated 25.9 million people in the United States have asthma, including approximately 7 million children.

**Cases:**

Cases are defined by a diagnostic history of one or more relevant asthma medications and a history of asthma as determined by ICD9 codes or chart review. The individual should be four years of age or older, have affirmative asthma ICD9 codes, (493.x) and have asthma been prescribed relevant medications.

Case inclusion criteria:

- Individuals 1460 days-old or older with one or more prescriptions of asthma related medications (see **Table 1**)

 *plus*

- Two or more relevant ICD9 codes in two or more in-person visits, on separate calendar days.

Case exclusion criteria:

- Individuals with any of the ICD9 codes shown in **Table 2**

**Note:** Smoking history—as defined by packs/day x years use—should, be captured (per Pacheco et al., 2009)1 where available. This is not an inclusion/exclusion criterion, however

**Stratification of cases:**

Stratified by presence or absence of allergies:

- Atopic: Individuals with ICD9 code 493.0 or two or more ICD9 codes in **Table 3** on separate calendar days

**Controls:**

 - Individuals 1460 days-old or older

 - No diagnosis codes for asthma (493.xx)

 - No history of relevant medications (see Table 1)

 - No exclusionary ICD 9 codes (see Table 4)

**Covariates:**

Age

 Gender

 Ethnicity

 Race

 BMI

 Pets in home

 Smoking status/smoke in home

 IgE test

 Positive RAST test

 Positive rhinoconjuctivitis

 History of Asthma medications

 History of Asthma diagnosis

**Table 1:**

|  |
| --- |
|  **Asthma medication by sub-type.**  |
| **Oral Steroids, anti-IgE** **(-> severe)** | **Inhaled Steroids** **(-> moderate)**  | **Beta-Agonists** **(-> mild)**  | **Other** **(-> mild)**  |
| Dexamethasone (Decadron, Deltasone)  | Beclomethasone (QVAR)  |  **β1 agonists** | **Mast cell stabilizers** |
| Methylprednisolone (Medrol, Medrol Dosepak)  | Budesonide (Pulmicort Turbuhaler, Pulmicort Respules) Budesonide-Formoterol | Methylxanthine | Cromolyn (Cromoglicic acid, cromoglycate, cromoglicate, Intal)Cromolyn Sodium |
| Prednisone (Orasone)  | Flunisolide (Aerobid, Pulmicort Respules)  | Theophylline (aminophylline, Dimethylxanthine, Slo-Bid, Theo, Theodur, Theolair, Uniphyl)  | Nedocromil (Alocril, Rapitil, Tilade)  |
| Prednisolone (Orapred, Pediapred, Prelone)  | Fluticasone (Flovent), Fluticasone-salmeterol (Advair) Fluticasone propionate HFA, Fluticasone Propionate inhaled | Xamoterol | **Leukotriene-Antagonists** |
| Triamcinolone (Aristocort) | Mometasone (Asmanex Twisthaler) Mometasone-formoterol (Dulera) | **β2 agonists** | Montelukast |
| **Anti IgE:**  | Triamcinolone(Azmacort)Triamcinolone Acetonide  | Arformoterol (Brovana, Sunovion, )  | Zafirlukast |
| Omalizumab (Xolair) | Ciclesonide | Albuterol, Albuterol Sulfate (Salbutamol, Ventolin, Proventil, ProAir, Accuneb)  | Zileuton  |
|  |  | Clenbuterol  | **Ipratropium Bromide** |
|  |  | Fenoterol  | Aerovent |
|  |  | Formoterol (Foradil) | Apovent |
|  |  | Isoetarine | Atrovent |
|  |  | Levalbuterol, Levalbuterol HCL, Levalbuterol Tartrate (Levosalbutamol, Xopenex) | Ipraxa |
|  |  | Metaproterenol | **Phosphodiesterase Inhibitors**  |
|  |  | Pirbuterol (Maxair) | Ibudilast |
|  |  | Procaterol  |  |
|  |  | Ritodrine  |  |
|  |  | Salmeterol (Serevent)  |  |
|  |  | Terbutaline (Brethine) |  |
|  |  | Ipratropium-Albuterol |  |

**Table 2:**

|  |
| --- |
| **Asthma Exclusionary ICD9 Codes.**  |
| **ICD-9 Codes** | **Diagnosis**  |
| **General** |
| 273.4 | Alpha 1- antitrypsin deficiency |
| 277.xx | Cystic Fibrosis |
| 415.x | Acute Pulmonary Heart Disease |
| 416.x | Chronic Pulmonary Heart Disease |
| 478.3xx | Vocal Cord Dysfunction  |
| 478.5 | Paradoxical Vocal Cord Motion |
| 492.xx | Emphysema |
| 494.xx | Bronchiectasis, Allergic Alveolitis |
| 495.2  | Bird-fanciers' lung |
| 496.xx | COPD  |
| 714 | Rheumatoid Arthritis |
| 748.5 | Agenesis, hypoplasia, and dysplasia of lung |
| 769.xx | Respiratory Distress Syndrome  |
| V81.3  | Chronic bronchitis and emphysema |
| **Transplant**  |
| **ICD-9 Codes** | **Diagnosis**  |
| 238.77 | Post-transplant lymphoproliferative disorder (PTLD) |
| 996.8  | Complications of transplanted organ |
| E878.0  | Surgical operation with transplant of whole organ |
| V42  | Organ or tissue replaced by transplant |
| V49.83  | Awaiting organ transplant status |
| V58.44  | Aftercare following organ transplant |

**Table 3:**

|  |
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| **ICD9 Codes Related to Allergies.**  |
| **ICD-9 Codes** | **Diagnosis**  |
| 287.0  | Allergic purpura |
| 372.14  | Other chronic allergic conjunctivitis |
| 477  | Allergic rhinitis |
| 495  | Extrinsic allergic alveolitis |
| 691.\* | Atopic dermatitis and related conditions |
| 708.0  | Allergic urticaria |
| 995.3  | Allergy, unspecified |
| V14  | Personal history of allergy to medicinal agents |
| V15.0 | Allergy, other than to medicinal agents |
| V15.01  | Allergy to peanuts |
| V15.03  | Allergy to eggs |
| V15.09  | Other allergy, other than to medicinal agents |
| V19.6  | Allergic disorders |

**Table 4:**

|  |
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| **Control Exclusionary ICD9 Codes.**  |
| **ICD-9 Codes** | **Diagnosis**  |
| 212.3 | BENIGN NEO BRONCHUS/LUNG |
| 238.77 | POST-TRANSPLANT LYMPHOPROLIFERATIVE DISOR (PTLD) |
| 273.4 | ALPHA 1 ANTITRYPSIN DEFICIENCY |
| 277 | CYSTIC FIBROS W/O ILEUS |
| 277.01 | CYSTIC FIRBOSIS W ILEUS |
| 277.02 | CYSTIC FIBROSIS WITH PULMONARY MANIFESTATION  |
| 277.03 | CYSTIC FIBROSIS W GASTROINTESTINAL MANIFEST |
| 277.09 | CYSTIC FIBROSIS WITH OTHER MANIFESTATIONS |
| 277.1 | DIS PORPHYRIN METABOLISM |
| 277.3 | AMYLOIDOSIS |
| 277.3 | AMYLOIDOSIS, UNSPECIFIED |
| 277.39 | OTHER AMYLOIDOSIS |
| 277.5 | MUCOPOLYSACCHARIDOSIS |
| 277.6 | DEFIC CIRCUL ENZYME NEC |
| 277.8 | METABOLISM DISORDER NEC |
| 277.87 | DISORDERS OF MITOCHONDRIAL METABOLISM |
| 277.88 | TUMOR LYSIS SYNDROME |
| 279.4 | AUTOIMMUNE DISEASE NEC |
| 283 | AUTOIMMUN HEMOLYTIC ANEM |
| 283.1 | NON-AUTOIMMUNE HEMOLYTIC ANEMIA UNSPEC |
| 283.11 | HEMOLYTIC-UREMIC SYNDROME  |
| 283.19 | OTHER NON-AUTOIMMUNE HEMOLYTIC ANEMIA  |
| 287 | ALLERGIC PURPURA |
| 372.14 | CHR ALLRG CONJUNCTIV NEC |
| 415 | ACUTE PULM HEART DIS |
| 415.0 | ACUTE COR PULM |
| 415.1 | PULM EMBOLISM AND INF |
| 415.11 | IATROGENIC PULM EMB AND INF |
| 415.12 | SEPTIC PULMONARY EMB |
| 415.13 | SADDLE EMBOLUS OF PULM ARTERY |
| 415.19 | OTHER PULM EMB AND INF |
| 416 | CHRONIC PULMONARY HEART DIS |
| 416.0 | PRIMARY PULMONARY HTN |
| 416.1 | KYPHOSCOLIOTIC HEART DIS |
| 416.2 | CHRONIC PULMONARY EMBOLISM |
| 416.8 | CHR PULMON HEART DIS NEC |
| 416.9 | CHR PULMON HEART DIS NOS |
| 464.11 | AC TRACHEITIS W OBSTRUCT |
| 464.3 | AC EPIGLOTTITIS NO OBSTR |
| 466.11 | ACUTE BRONCHIOLITIS DUE TO RSV |
| 472 | CHRONIC RHINITIS |
| 472 | ALLERGIC RHINITIS |
| 472.2 | CHRONIC NASOPHARYNGITIS |
| 474.01 | CHRONIC ADENOIDITIS |
| 474.2 | ADENOID VEGETATIONS |
| 476.1 | CHR LARYNGOTRACHEITIS |
| 477.1 | ALLERGIC RHINITIS, DUE TO FOOD |
| 477.2 | ALLERGIC RHINITIS, D/T ANIMAL HAIR & DANDER |
| 477.8 | ALLERGIC RHINITIS NEC |
| 477.9 | ALLERGIC RHINITIS NOS |
| 478.11 | NASAL MUCOSITIS (ULCERATIVE) |
| 478.21 | CELLULITIS OF PHARYNX |
| 478.22 | PARAPHARYNGEAL ABSCESS |
| 478.24 | RETROPHARYNGEAL ABSCESS |
| 478.25 | EDEMA PHARYNX/NASOPHARYX |
| 478.26 | CYST PHARYNX/NASOPHARYNX |
| 478.32 | VOCAL PARAL UNILAT TOTAL |
| 478.33 | VOCAL PARAL BILAT PART |
| 478.34 | VOCAL PARAL BILAT TOTAL |
| 478.74 | STENOSIS OF LARYNX |
| 478.8 | URT HYPERSENS REACT NOS |
| 478.9 | UPPER RESP DIS NEC/NOS |
| 480 | ADENOVIRAL PNEUMONIA |
| 480.1 | RESP SYNCYT VIRAL PNEUM |
| 480.2 | PARINFLUENZA VIRAL PNEUM |
| 480.8 | VIRAL PNEUMONIA NEC |
| 482 | K. PNEUMONIAE PNEUMONIA |
| 482.1 | PSEUDOMONAL PNEUMONIA |
| 482.3 | PNEUMONIA DUE TO STREPTOCOCCUS |
| 482.3 | PNEUMONIA DUE TO STREPTOCOCCUS, UNSPECIFIED |
| 482.31 | PNEUMONIA DUE TO GROUP A STREPTOCOCCUS |
| 482.39 | PNEUMONIA DUE TO OTHER STREPTOCOCCUS |
| 482.4 | STAPHYLOCOCCAL PNEUMONIA |
| 482.4 | PNEUMONIA DUE TO STAPHYLOCOCCUS, UNSPECIFIED  |
| 482.42 | METHICILLIN RESIST PNEUMONIA DUE TO STAPH AUREUS |
| 482.8 | PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA |
| 482.81 | PNEUMONIA DUE TO ANAEROBES |
| 482.82 | PNEUMONIA DUE TO ESCHERICHIA COLI |
| 482.83 | PNEUMONIA DUE TO OTHER GRAM-NEGATIVE BACTERIA |
| 482.84 | LEGIONNAIRES' DISEASE |
| 482.89 | PNEUMONIA DUE TO OTHER SPECIFIED BACTERIA |
| 483.1 | PNEUMONIA DUE TO CHLAMYDIA |
| 483.8 | PNEUMONIA DUE TO OTHER SPECIFIED ORGANISM |
| 484.1 | PNEUM W CYTOMEG INCL DIS |
| 484.3 | PNEUMONIA IN WHOOP COUGH |
| 484.6 | PNEUM IN ASPERGILLOSIS |
| 484.7 | PNEUM IN OTH SYS MYCOSES |
| 484.8 | PNEUM IN INFECT DIS NEC |
| 488 | INFLUENZA DUE TO IDENTIFIED AVIAN INFLUENZA VIRUS |
| 488.1 | INFLUENZA DUE TO H NINFLUENZA VIRUS |
| 491.2 | OBSTRUCTIVE CHRONIC BRONCHITIS W/O EXACERBAT |
| 491.22 | OBSTRUCTIVE CHRONIC BRONCHITIS WITH AC BRONC |
| 491.8 | CHRONIC BRONCHITIS NEC |
| 492.8 | EMPHYSEMA NEC |
| 494 | BRONCHIECTASIS |
| 494 | BRONCHIECTASIS W/O ACUTE EXACERBATION |
| 494.1 | BRONCHIECTASIS WITH ACUTE EXACERBATION |
| 495 | FARMERS' LUNG |
| 495 | MYCOTOXICOSIS/ORGANIC DUST TOXIC SYNDROME |
| 495.1 | BAGASSOSIS |
| 495.2 | BIRD-FANCIERS' LUNG |
| 495.5 | MUSHROOM WORKERS' LUNG |
| 495.8 | ALLERG ALVEOL/PNEUM NEC |
| 495.9 | ALLERG ALVEOL/PNEUM NOS |
| 496 | CHR AIRWAY OBSTRUCT NEC |
| 496 | CHR AIRWAY OBSTRUCT NEC |
| 500 | COAL WORKERS' PNEUMOCONIOSIS |
| 500 | COAL WORKERS' PNEUMOCON |
| 501 | ASBESTOSIS |
| 502 | SILICA PNEUMOCON NEC |
| 503 | INORG DUST PNEUMOCON NEC |
| 505 | PNEUMOCONIOSIS NOS |
| 505 | PNEUMOCONIOSIS NOS |
| 506 | FUM/VAPOR BRONC/PNEUMON |
| 506.1 | FUM/VAPOR AC PULM EDEMA |
| 506.2 | FUM/VAPOR UP RESP INFLAM |
| 506.3 | FUM/VAP AC RESP COND NEC |
| 506.4 | FUM/VAPOR CHR RESP COND |
| 507.1 | OIL/ESSENCE PNEUMONITIS |
| 507.8 | SOLID/LIQ PNEUMONIT NEC |
| 508.1 | CHR PUL MANIF D/T RADIAT |
| 508.8 | RESP COND: EXT AGENT NEC |
| 508.9 | RESP COND: EXT AGENT NOS |
| 510 | EMPYEMA WITH FISTULA |
| 511.1 | BACT PLEUR/EFFUS NOT TB |
| 511.81 | MALIGNANT PLEURAL EFFUSION |
| 512 | SPONT TENS PNEUMOTHORAX |
| 512.89 | OTHER PNEUMOTHORAX |
| 513.1 | ABSCESS OF MEDIASTINUM |
| 516.1 | IDIO PULM HEMOSIDEROSIS |
| 516.31 | IDIOPATHIC PULMONARY FIBROSIS |
| 516.34 | RESPIRATORY BRONCHIOLITIS INTERSTITIAL LUNG DIS |
| 516.4 | LYMPHANGIOLEIOMYOMATOSIS |
| 516.5 | ADULT PULMONARY LANGERHANS CELL HISTIOCYTOSIS |
| 516.8 | BRONCHIOLITIS OBLITERANS WITH ORGANIZING PNEUMONIA |
| 516.9 | ALVEOL PNEUMONOPATHY NOS |
| 517.1 | RHEUMATIC PNEUMONIA |
| 517.2 | SYST SCLEROSIS LUNG DIS |
| 518.1 | INTERSTITIAL EMPHYSEMA |
| 518.51 | ACUTE RESPIRATORY FAILURE FOLLOW TRAUMA & SURGERY |
| 518.52 | OTH PULMONARY INSUFFIC, NEC, FOLLOW TRAUMA & SURG |
| 518.6 | ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS |
| 518.7 | TRANSFUSION RELATED ACUTE LUNG INJURY (TRALI) |
| 518.801 | COIN LESION LUNG |
| 518.81 | RESPIRATORY FAILURE ACUTE |
| 518.811 | RESPIRATORY FAILURE CHRONIC |
| 518.89 | SOLITARY PLUMONARY NODULE |
| 519 | TRACHEOSTOMY COMPLIC |
| 519 | UNSPECIFIED TRACHEOSTOMY COMPLICATION |
| 519.01 | INFECTION OF TRACHEOSTOMY |
| 519.02 | MECHANICAL COMPLICATION OF TRACHEOSTOMY |
| 519.09 | OTHER TRACHEOSTOMY COMPLICATION |
| 519.11 | ACUTE BRONCHOSPASM |
| 519.2 | MEDIASTINITIS |
| 519.3 | MEDIASTINUM DISEASE NEC |
| 519.6 | DELETED |
| 519.8 | RESP SYSTEM DISEASE NEC |
| 519.9 | RESP SYSTEM DISEASE NOS |
| 519.9 | RECURRENT RESPIRATORY INFECTIONS |
| 525.66 |  ALLERGY TO EXISTING DENTAL RESTORATIVE MATERIAL |
| 555 | REG ENTERITIS, SM INTEST |
| 556 | IDIOPATHIC PROCTOCOLITIS |
| 556 | ULCERATIVE ENTEROCOLITIS  |
| 571.42 | AUTOIMMUNE HEPATITIS |
| 708 | ALLERGIC URTICARIA |
| 714 | RHEUMATOID ARTHRITIS |
| 748.4 | CONGENITAL CYSTIC LUNG |
| 748.5 | AGENESIS OF LUNG |
| 751.61 | BILIARY ATRESIA |
| 769 | RESPIRATORY DISTRESS SYN |
| 769 | RESPIRATORY DISTRESS SYN |
| 995.3 | ALLERGY, UNSPECIFIED |
| 996.8 | COMPLICATIONS OF TRANSPLANTED ORGAN |
| E878.0 | E ABN REACT-ORG TRANSPLANT |
| V14 | PERSONAL HISTORY OF ALLERGY TO MEDICINAL AGENTS |
| V15.0 | V HX OF ALLERGY NEC |
| V15.01 | V ALLERGY TO PEANUTS |
| V15.03 | V ALLERGY TO EGGS |
| V15.09 | V OTHER ALLERGY, OTH THAN TO MEDICINAL AGENTS |
| V19.6 | V FAMILY HX-ALLERGIC DIS |
| V42 | ORGAN OR TISSUE REPLACED BY TRANSPLANT |
| V49.83 | V AWAITING ORGAN TRANSPLANT STATUS  |
| V58.44 | V AFTERCARE FOLLOWING ORGAN TRANSPLANT |

The attached data dictionary defines the values that should be returned. The flow chart, below, provides an outline of the algorithm and relevant analytical components.

EMRs

Race

BMI

Zip code

Diagnostic Criteria

for

include

If No, exclude

Yes

No

Mild

Moderate

Severe

Atopic

Non-Atopic

Asthma ICD Codes

if No, check for

Beta-Agonists

Allergies

Steroids

ER Visits

include

Inhaled

Cases

Yes

Controls

Autoimmune Diseases

Cystic Fibrosis

Bronchiectasis

PCD

COPD

Transplants

Chart Review

plus

 IgE levels

Duration of disease

RAST test

**References:**

1. Pacheco JA, Avila PC, Thompson JA, Law M, Quraishi JA, Greiman AK, Just EM, Kho A. A highly specific algorithm for identifying asthma cases and controls for genome-wide association studies. *AMIA Annu Symp Proc*. 2009 Nov 14; 2009:497-501.