CHECK

Connecting Families. Supporting Health.

Coordination of Healthcare for Complex Kids

Accessing Specialty Asthma Care: Barriers, Solutions and New Directions in Therapy

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Objectives

- Discuss access to care barriers and novel ways to mitigate them
- Define effective strategies to prevent exacerbations and prevention of disease
- New directions in pediatric asthma management

Barriers

Non-Adherence

- Complexity of Regimen
- Perceived Risk
- Costs
- Side effects
- Health Literacy
- Poor ability to recognize symptoms
- Socioeconomic strain

Canino, et al JACI 2009

Barriers to Specialty Care

Table 2. Likelihood of Being Denied a Scheduled Specialty Care Appointment According to Type of Insurance.*

Specialty	Total Clinics Called†	Both Insurance Types Denied	Both Insurance Types Accepted	Public Insurance Denied and Private Insurance Accepted	Public Insurance Accepted and Private Insurance Denied	Odds Ratio for Appointment Denial with Public Insurance (95% CI)‡	Public Insurance Denied	Private Insurance Denied	Relative Risk of Appointment Denial with Public Insurance (95% CI)‡
		number (percent)					*percent*		
All specialties	273	24 (8.8)	89 (32.6)	155 (56.8)	5 (1.8)	31.0 (13.0–96.8)	65.6	10.6	6.2 (4.3–8.8)
Orthopedics	40	1 (0.4)	8 (2.9)	31 (11.4)	0	44.2 (7.9–∞)§	80.0	2.5	32.0 (4.6–223.0)
Dermatology	45	2 (0.7)	13 (4.8)	30 (11.0)	0	42.8 (7.6–∞)§	71.1	4.4	16.0 (4.1–62.8)
Otolaryngology¶	43	0	16 (5.9)	27 (9.9)	0	38.5 (6.8–∞)§	62.8	0	—
Asthma¶	44‖	0	20 (7.3)	24 (8.8)	0	34.1 (6.0–∞)§	54.5	0	—
Neurology	37	2 (0.7)	15 (5.5)	18 (6.6)	2 (0.7)	9.0 (2.2–79.9)	54.1	10.8	5.0 (1.9–13.2)
Endocrinology	23	1 (0.4)	12 (4.4)	9 (3.3)	1 (0.4)	9.0 (1.2–394.5)	43.5	8.7	5.0 (1.2–20.4)
Psychiatry	41	18 (6.6)	5 (1.8)	16 (5.9)	2 (0.7)	8.0 (1.9–71.7)	82.9	48.8	1.7 (1.2–2.4)

* Public insurance was reported by callers as the Illinois Medicaid–Children's Health Insurance Program (CHIP) umbrella program; private insurance was reported by callers as Blue Cross Blue Shield.
† All 273 clinics were called twice (for a total of 546 calls), once reporting Medicaid–CHIP coverage and once reporting private coverage.
‡ P<0.05 for all comparisons. Odds ratios were calculated with the use of McNemar's test to compare proportions of appointments for paired calls to the same clinic for children with public insurance versus those with private insurance. Relative risks, which were calculated for unpaired calls, are based on the overall appointment rates for children with public insurance versus those with private insurance.
§ Because of an extreme split on the dependent variable for orthopedics, asthma, otolaryngology, and dermatology, exact conditional (fixed-effects) logistic-regression odds ratios are medium unbiased estimates with no upper limit of the 95% confidence interval.
¶ Relative risks could not be calculated because there were no denials of care for children with private insurance.
‖ The asthma clinics included 38 allergy–immunology clinics and 6 pulmonary disease clinics.

Bisgauer, et al NEJM 2011

Barriers to Specialty Care

- ACCESS
  - Clinics not accepting Medicaid/state insurance
    - 66% denial with state insurance with only 11% on private insurance
  - Difficulty making appointments
  - Location of clinics
  - Absence of Referrals
    - Minority
    - Educational level
    - Gender
    - Income
- Psychosocial barriers

Bellinger, et al In J Env Resp Pub Health 2010

Specialty Care in Asthma

- Restricted Access to asthma specialists associated with
  - Higher rates of hospitalization
  - ED use
  - Increased risk of mortality
- May contribute to disparities in asthma morbidity

1-Canino, et al. JACI 2009, 2-Berman, et al Pediatrics 2005, 3-Joseph, et al JACI 1998,
4-Finkelstiein, et al, Arch Pediatr Adoles Med 2002

Barriers to Guideline Implementation

Provider and Others

- Personal Factors
  - Knowledge
  - Attitudes
- Guideline-based Factors
  - Plausibility/Applicability
  - Complexity
  - Co-morbidities
  - Evidence
- External Factors
  - Organizational Constraints
  - Lack of Resources
  - Lack of Collaboration
  - Social/Clinical Norms

Patient

- Lack of time
- Lack of money
- Insufficient involvement in therapy choices
- Quality of Life
- Communication barriers
- Mental health of chronic condition
- Greater empowerment
- More time needed

1-Fischer, et al Healthcare 2016 2-Lingner, et al BMC Pulm Health 2017

Communication Barriers

Martin, et al JACI 2016

Novel Ways to Improve Access

Navigating Disparities and Barriers

- Electronic Monitoring Devices[1]
- Technology [1]
- Comprehensive Programs like CHECK
- Mobile Care
- School Partnerships and School-based asthma programs

Anderson and Szefler, JACI 2015

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Coordination of Healthcare for Complex Kids

CHECK Mission

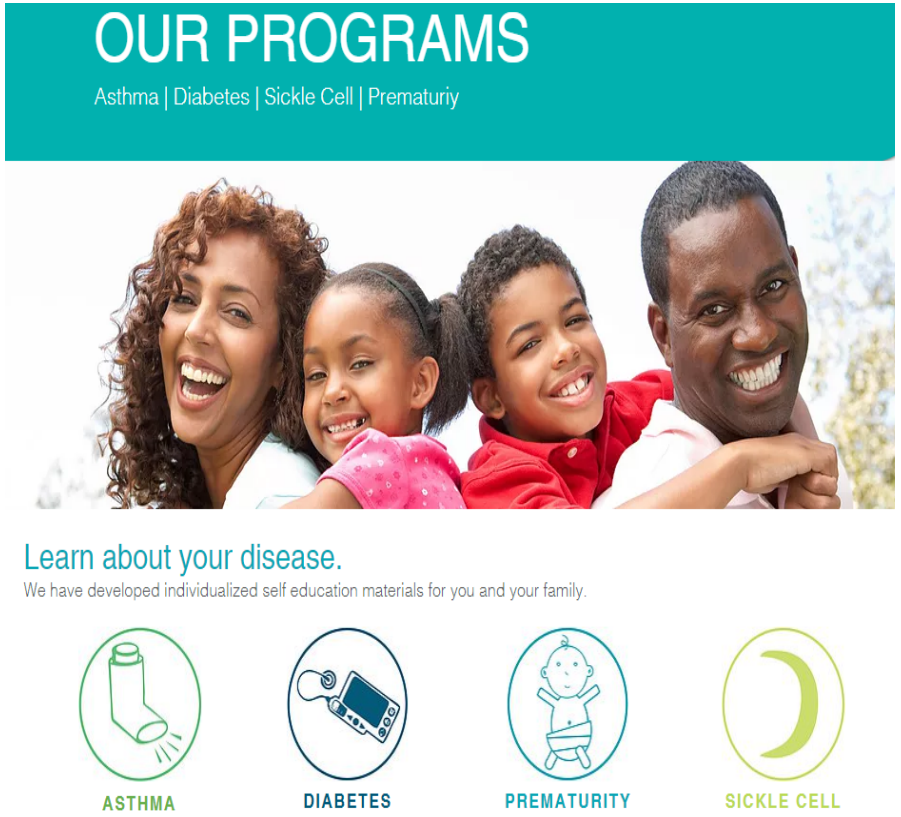
- Our mission is to improve the coordination of health care for children and young adults with chronic conditions by **engaging and collaborating** with them, their **families**, and their **communities** to provide tailored disease specific programs and to reduce their barriers to accessing medical, behavioral, and social services.

CHECK's Aims

- **Aim #1:** Reduce Health Care Costs
- **Aim #2:** Reduce School Asthma Absenteeism
- **Aim #3:** Increase Patient/Family Engagement

Enhanced Care Coordination

- <u>Community Health Workers (CHW)</u>
  - 30 CHWs
  - Help families navigate the healthcare system
  - Link multiple sectors in the community with the family
  - Support Psychosocial Needs
  - Help improve chronic disease management



CHECK Services

- Social Service Referrals
  - Mental Health Promotion Team
- Community Medical Neighborhood
  - Clinic and Social Services
  - 13 clinical partners
  - 15 non-clinical partners
- Disease Specific Programs
  - Asthma
  - Sickle Cell Disease
  - Diabetes
  - Prematurity
  - Oral Health
  - Mental Health

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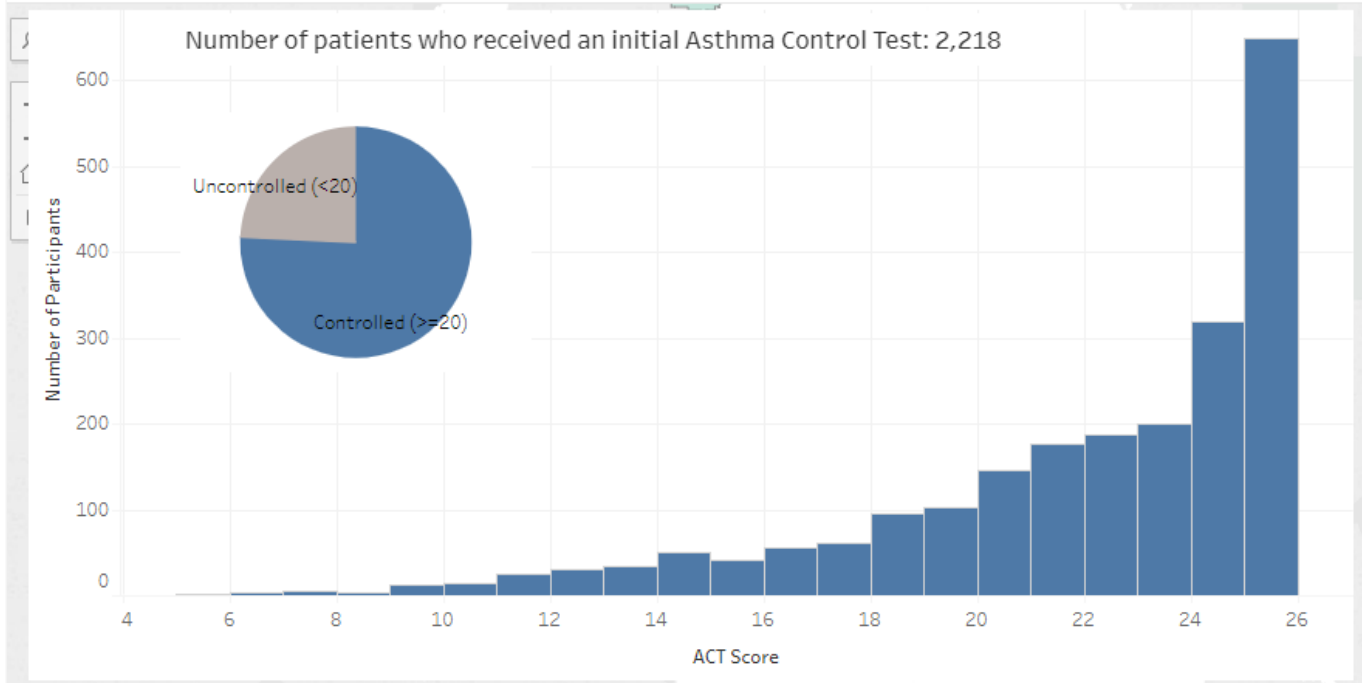
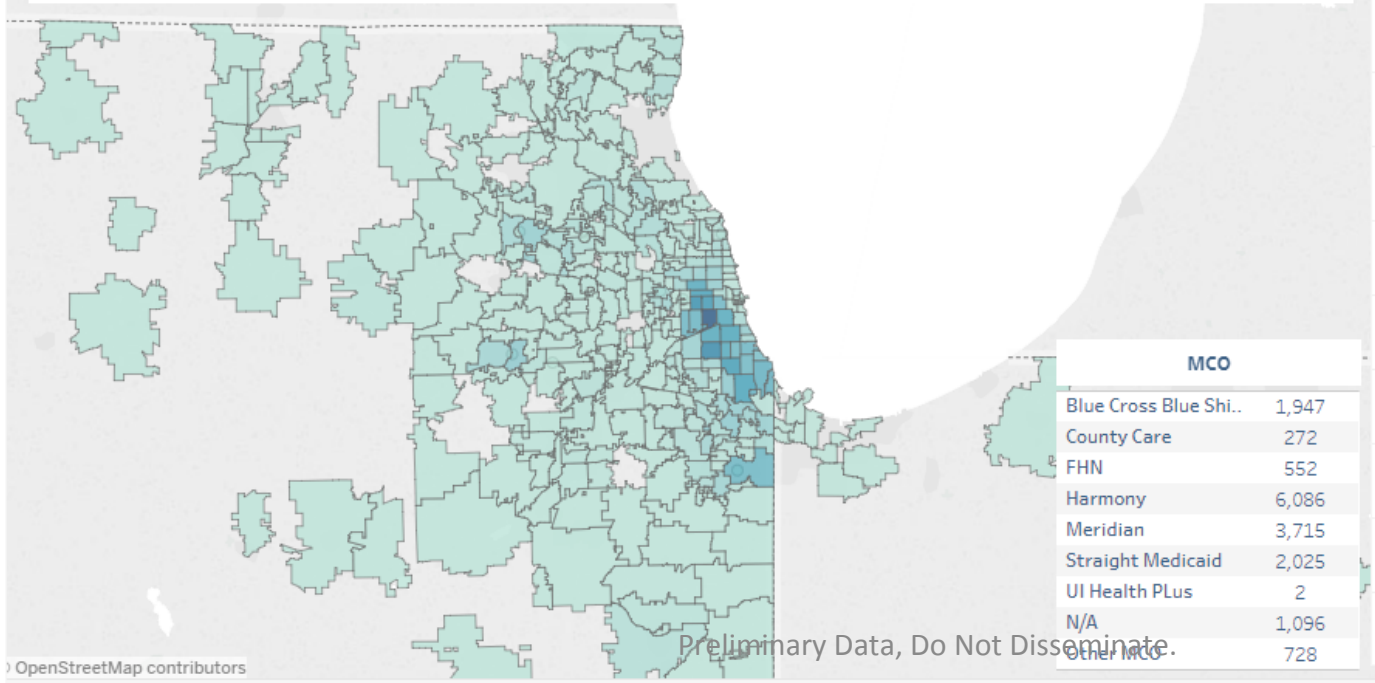
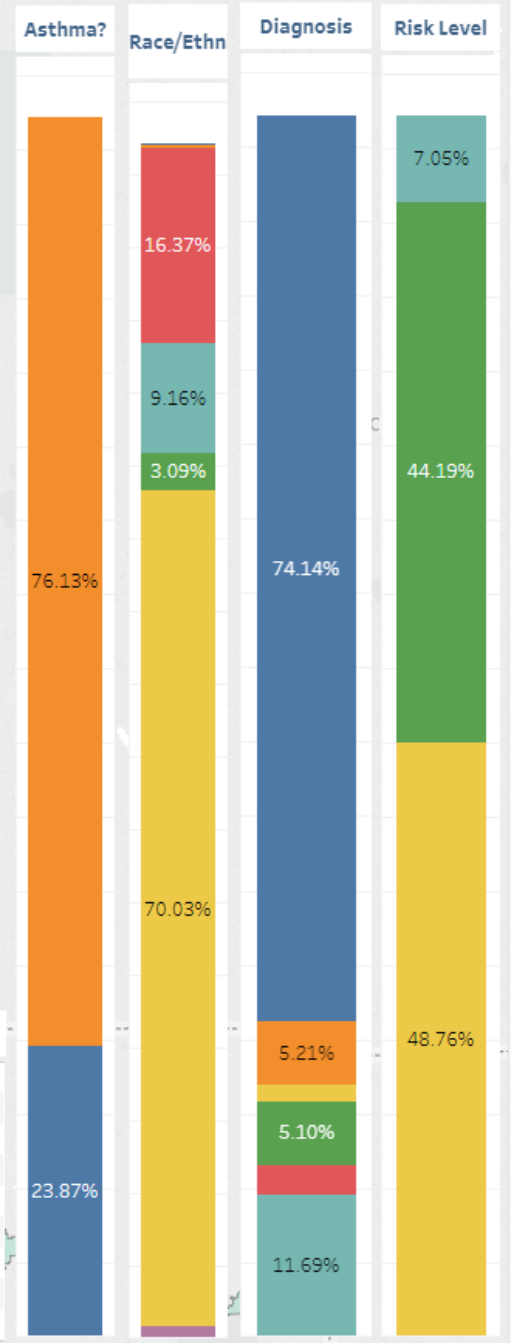
- 7,635 Enrolled
  - 5,971 Engaged
  - 80% cohort with asthma
- Age 0-25
  - Spans childhood, adolescence, early adulthood

- Risk Level
  - 7% High Risk
  - 51% Medium Risk
  - 41% Low Risk





MCO	
Blue Cross Blue Shi..	1,947
County Care	272
FHN	552
Harmony	6,086
Meridian	3,715
Straight Medicaid	2,025
UI Health PLus	2
N/A	1,096
Other MCO	728



Social Service Referrals

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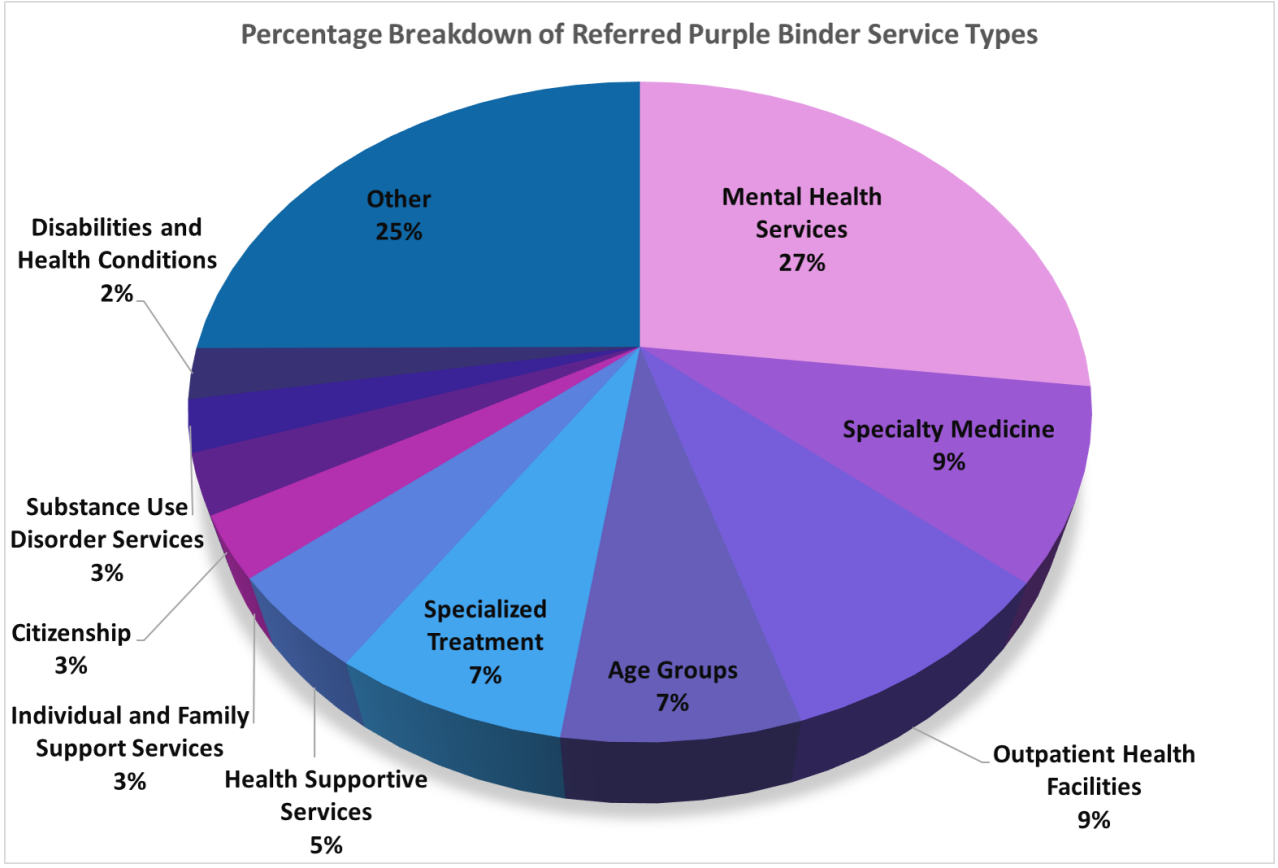
Total Referrals

n = 4,124



Data

- School
  - Reduction in missed school days
  - Reduction in Chronically Absent children

- Healthcare Costs
  - Reduced health care expenditures seen in Engaged Cohort
  - Reduction in ED visits
  - Reduction in hospitalizations

- 95% with a care plan in Engaged Cohort

Mobile Specialty Care

- Created in 1998
- Partnered with 40 Chicago-area schools
- 1/25 Mobile C.A.R.E patients report an ER visit or hospitalization since joining Mobile CARE in last year.
- Health Cost Reduction of 156 million over 13 years
- Allergist on Van

School-Based Asthma Interventions

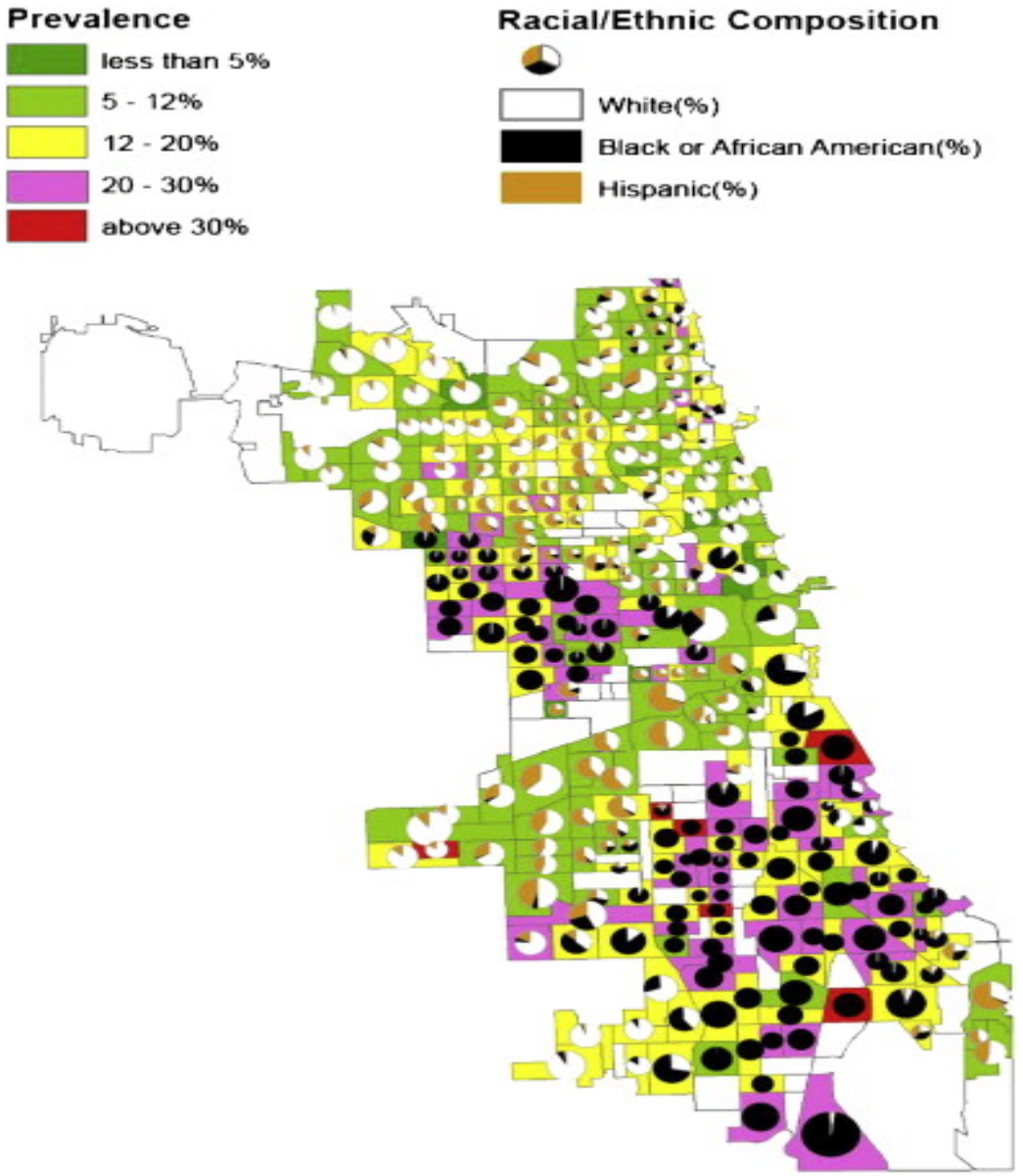
- <u>School-based Asthma Management Program (SAMPRO)</u>
  - AAAAI effort with multiple stakeholders (National Association of School Nursing, EPA, etc)
  - Four Components:
    - Circle of Support
    - Standardized Asthma Action and Treatment Plan
    - Asthma Education
    - Environmental Asthma Plan
- <u>Denver Public Schools</u>
  - Step Up Asthma Program, multi-disciplinary program
  - Used “Asthma Counselors” as a bridge
  - Improvements seen in multiple fields

1-Kukamanu, et al JACI 2016 2-Liptzin, et al JACI-IP 2016

Asthma Status and Prevention

Prevalence-Children

- Asthma Neighborhoods[1]
- Asthma Prevalence in Chicago AA Children ≈ 20%[1]
- National Asthma Prevalence
  - White: 7.4-8.2% (no change)[2]
  - AA: 11.4-16.8% (increasing 3.6%/year from 2001 to 2010)[2]
  - After 2010, increase less in AA, but poor children still increasing[3]



*The size of the race/ethnicitiy circles are based on the size of the neighborhood and are not representative of sample size
**Two hundred and eighty-seven neighborhoods with greater than 15 children from our sample were included in the analysis

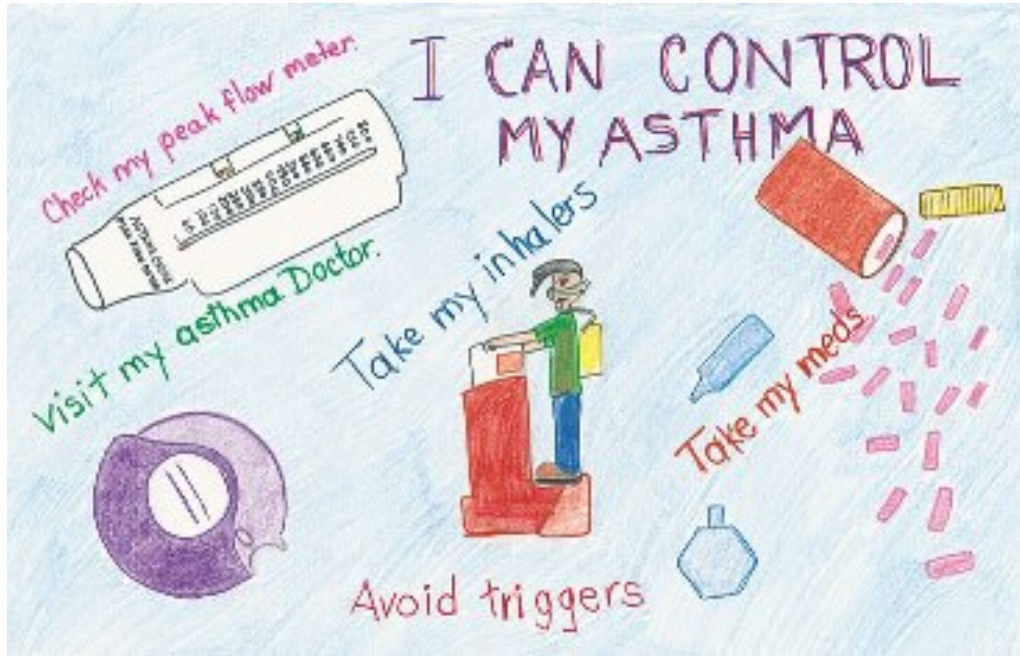
1- Gupta, et al JACI 2008 2-Akinambi, et al JACI 2014 3-Akinambi, Pediatrics 2016

Age of asthma diagnosis

- 1993: 4.7 years
- 2000: 2.6 Years
  - 35.6%-45.2% asthma into adulthood
  - Most have lung function abnormalities
  - Early onset asthma:
    - Increased airway obstruction than non-asthmatics
    - Persistent Pediatric wheezing
      - Reduces Lung Function
      - Reduces FEV1 growth over adolescents
  - Severe childhood asthma
    - Continued active disease as adulthood likely

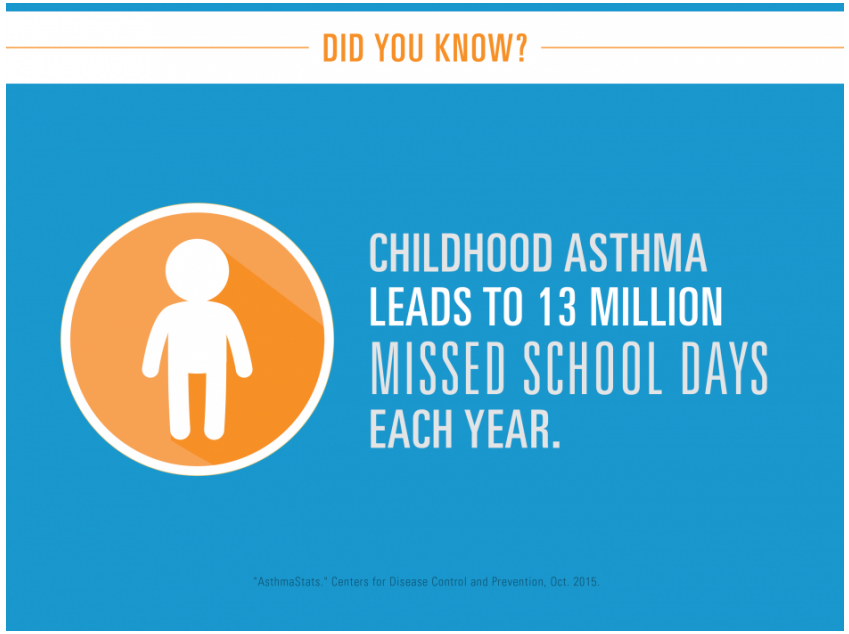
Can we prevent asthma?

NO THERAPY PREVENTS DEVELOPMENT OF PEDIATRIC ASTHMA



Can we prevent PROGRESSION?

Children with Persistent asthma:



- ↑ exacerbations
- ↑ hospitalizations
- ↑ ED visits
- ↑ Oral Corticosteroid Use
- ↑ Progressive loss of Lung Function

Controlled asthma can prevent symptoms leading to worsening

But cannot always adequately address underlying problem in subset of patients

New Directions in Asthma Therapy

Inhaled Therapies

New Thoughts on Inhaled Options

- We know inhaled corticosteroids work, but there are issues[1]:
  - Reduction of Growth Velocity
  - Potential hypothalamic-pituitary-adrenal axis suppression
- Pediatric LABA use based mostly on adult data[1]
  - Recent data does demonstrate safety[2]
- Question whether on demand ICS better in some patients than continuous
  - Wheezy toddlers population [3]
- ICS/LABA for both maintenance and reliever?
  - Budesonide/formoterol formulation[4]

1-Anderson, JACI 2015, 2-Stempel, et al NEJM 2016, 3-Zeiger, et al NEJM 2011, Martinez, et al Lancet 2011, 4-O'Byrne, et al AM J Respir Crit Care Med 2005.

New ICS/LABA Combinations

- Once daily ICS and ICS/LABA combinations
- “Triple Therapy”
  - ICS/LABA and anti-cholinergics

Tiotropium

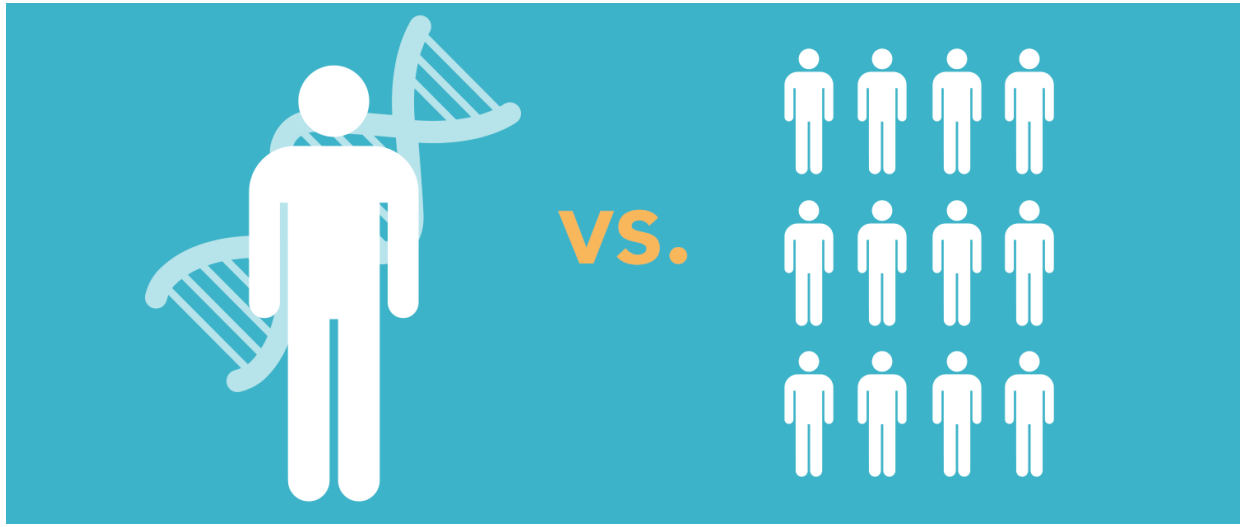
- Long acting anti-cholinergic
- Improves lung function, quality of life and exacerbations in COPD
  - TALC trial adding tio to ICS instead of doubling dose of ICS was superior and non-inferior to salmeterol addition[1]
  - Similar results in persistent asthma in adults with decrease exacerbations[2]
  - Children improved FEV1, PEF[3]
- Respimat an easy to use device
- Now approved in children 6 and up

1-Peters, et al NEJM, 2010 2-Kerstjens, et al Lance Resp Med 2015, 3- Vogelberg, et al Respir Med 2015

Precision Medicine

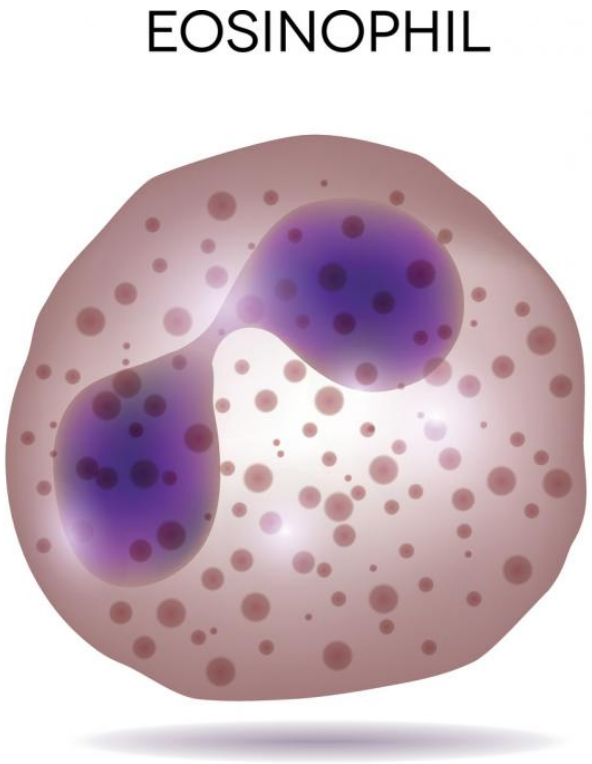
What is Precision Medicine?

- Medical model that proposes the customization of healthcare, with medical decisions, practices, and/or products being tailored to the individual patient
- Better prediction of response to treatment, risk prediction, disease modifying effects



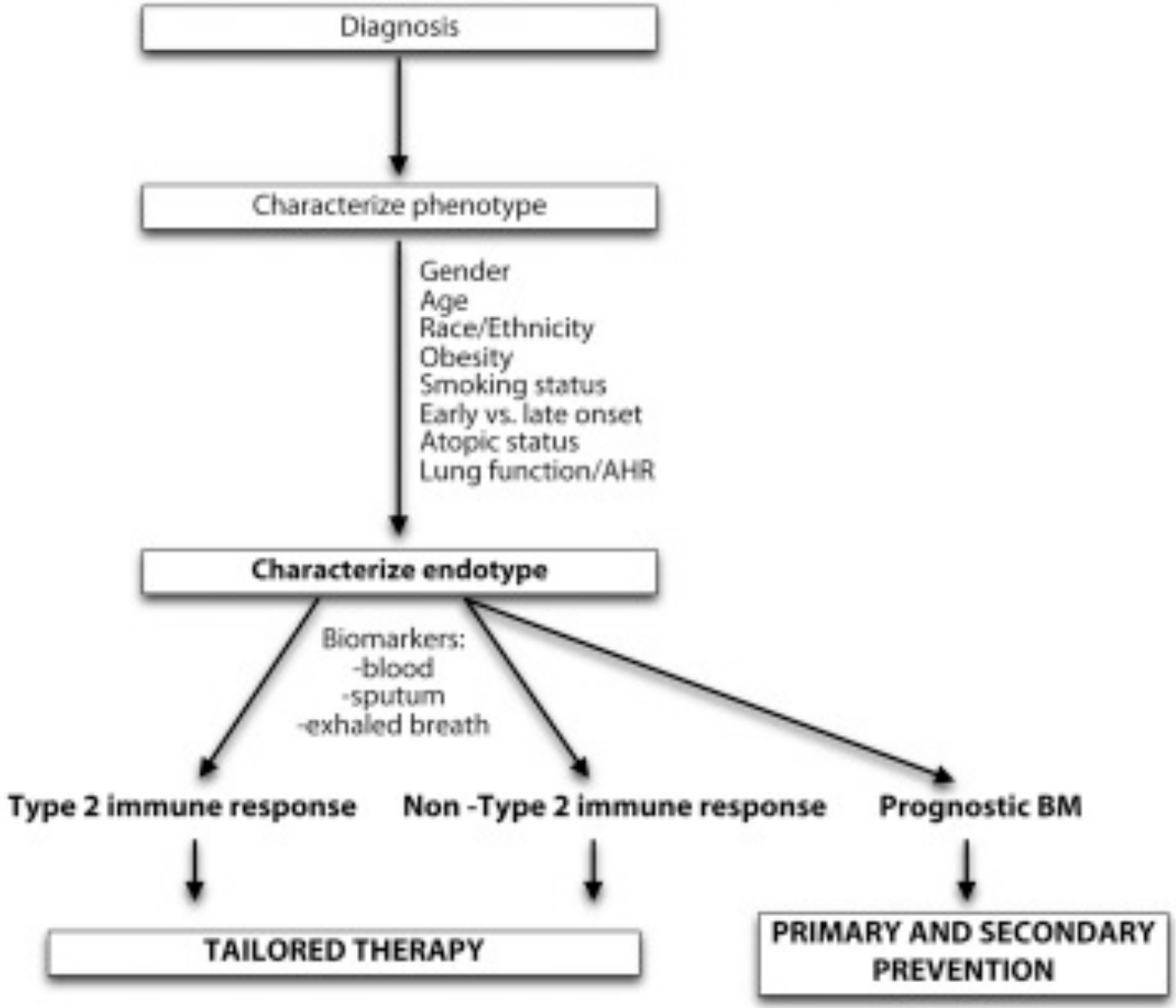
Biomarkers, Phenotypes, Endotypes

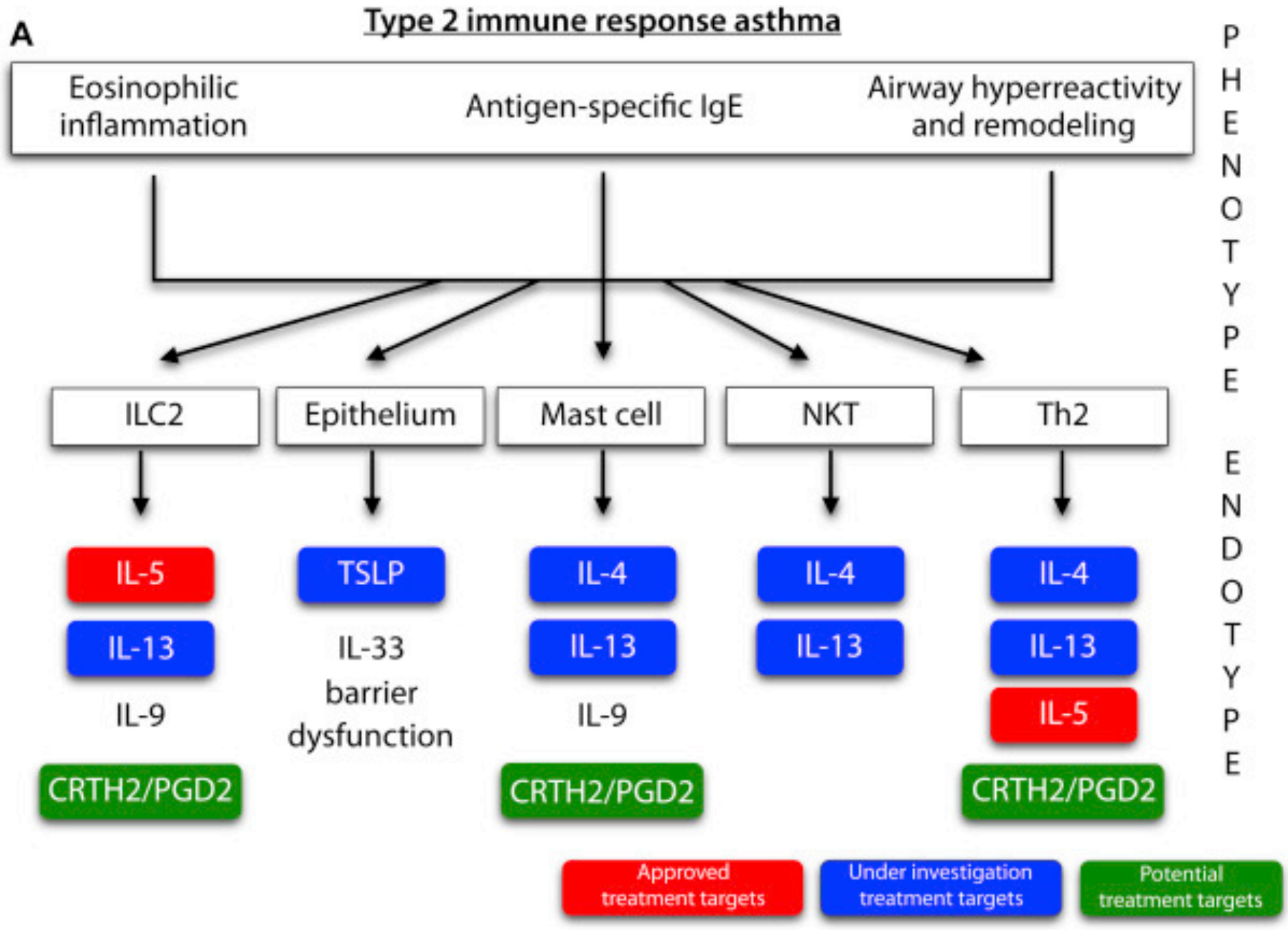
Definitions

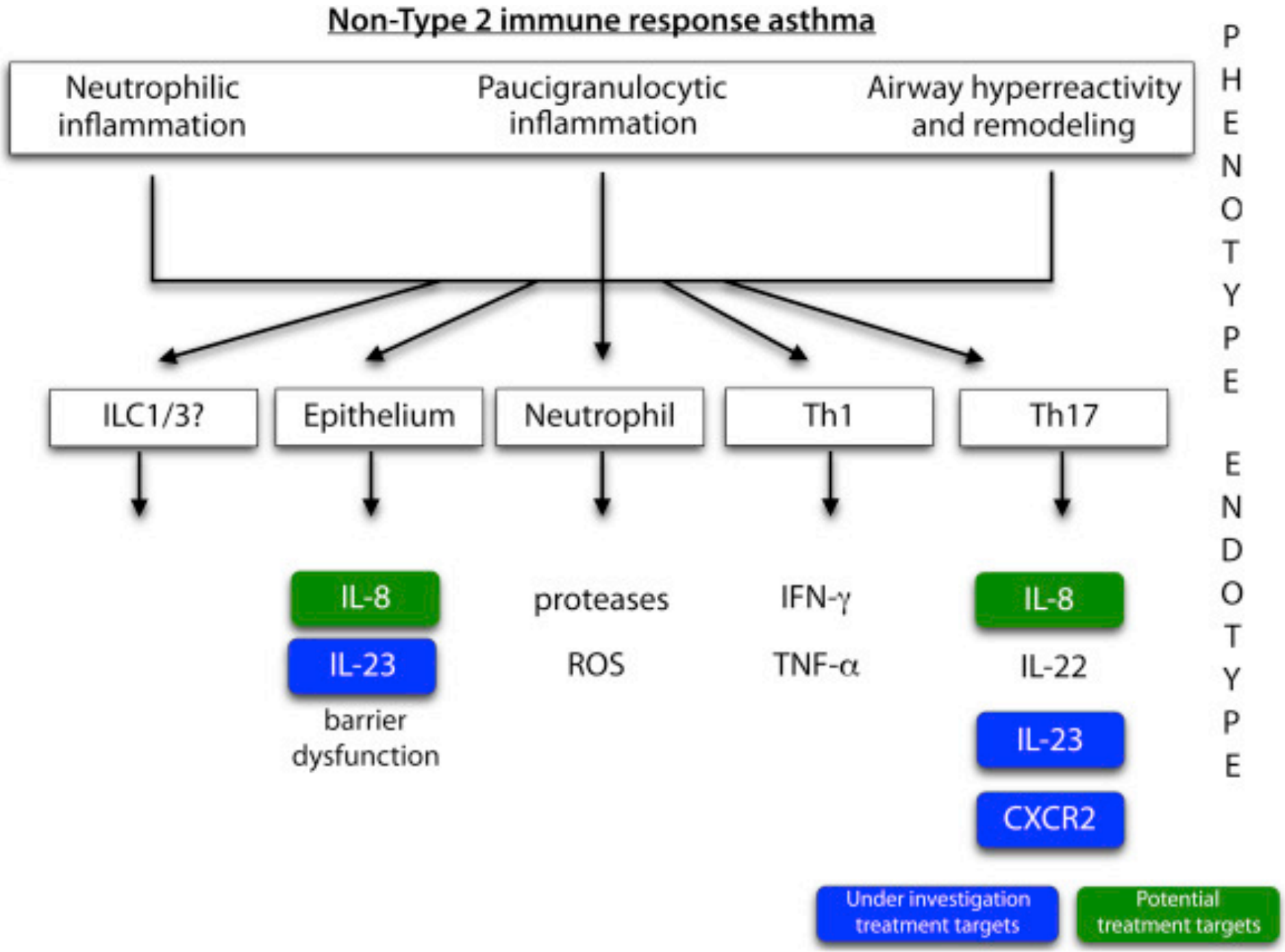


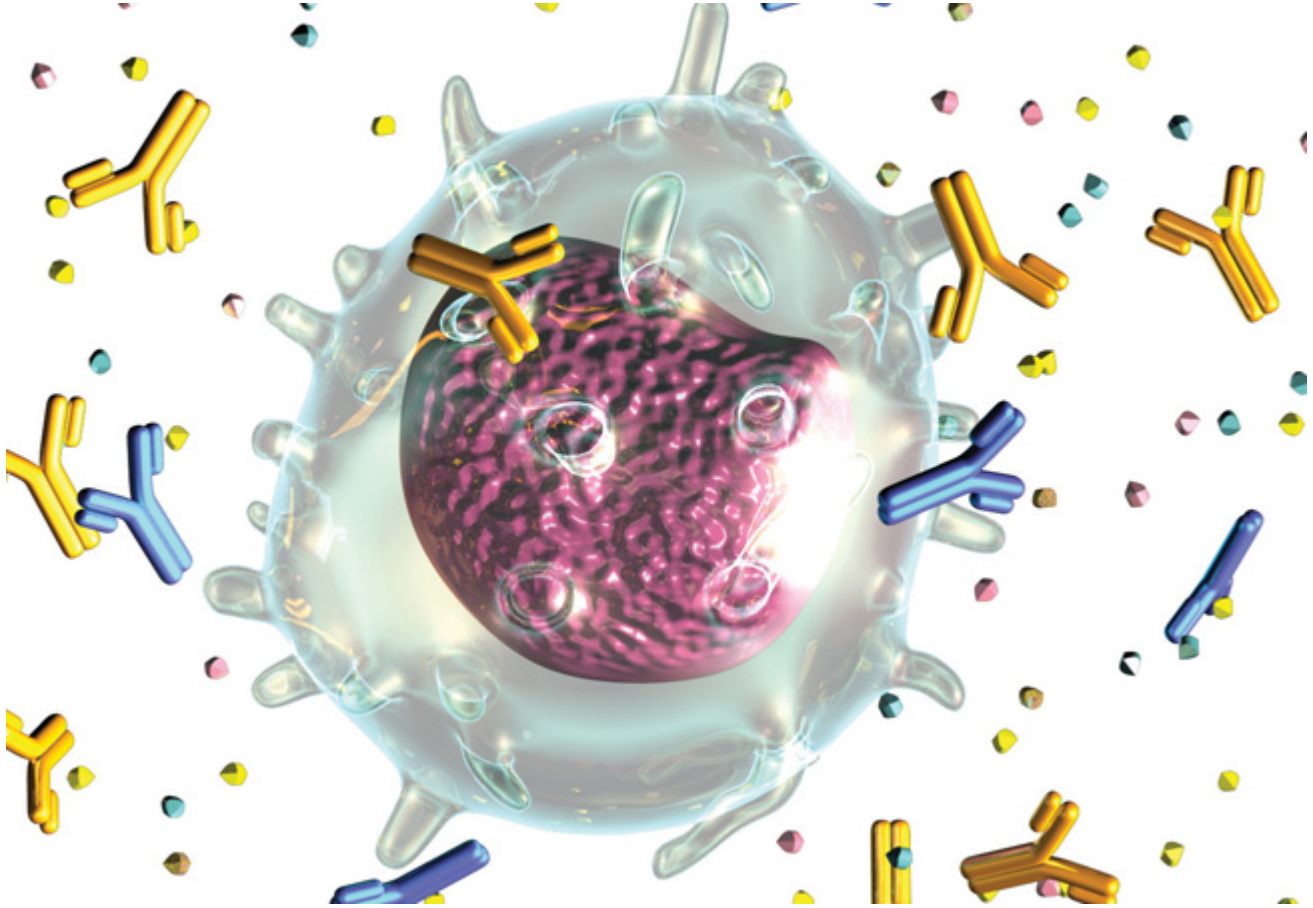
- Biomarker:
  - Objective measurements observed from outside the patient
- Phenotype:
  - Patient's characteristics
- Endotype:
  - Underlying pathogenic mechanism

Suggested approach to precision medicine in asthma




A
Type 2 immune response asthma
Eosinophilic inflammation
Antigen-specific IgE
Airway hyperreactivity and remodeling
PHENOTYPE
ILC2
Epithelium
Mast cell
NKT
Th2
ENDOTYPE
IL-5
IL-13
IL-9
CRTH2/PGD2
TSLP
IL-33
barrier dysfunction
IL-4
IL-13
IL-9
CRTH2/PGD2
IL-4
IL-13
IL-4
IL-13
IL-5
CRTH2/PGD2
Approved treatment targets
Under investigation treatment targets
Potential treatment targets


Non-Type 2 immune response asthma
Neutrophilic inflammation
Paucigranulocytic inflammation
Airway hyperreactivity and remodeling
PHENOTYPE
ILC1/3?
Epithelium
Neutrophil
Th1
Th17
ENDOTYPE
IL-8
IL-23
barrier dysfunction
proteases
ROS
IFN-γ
TNF-α
IL-8
IL-22
IL-23
CXCR2
Under investigation treatment targets
Potential treatment targets

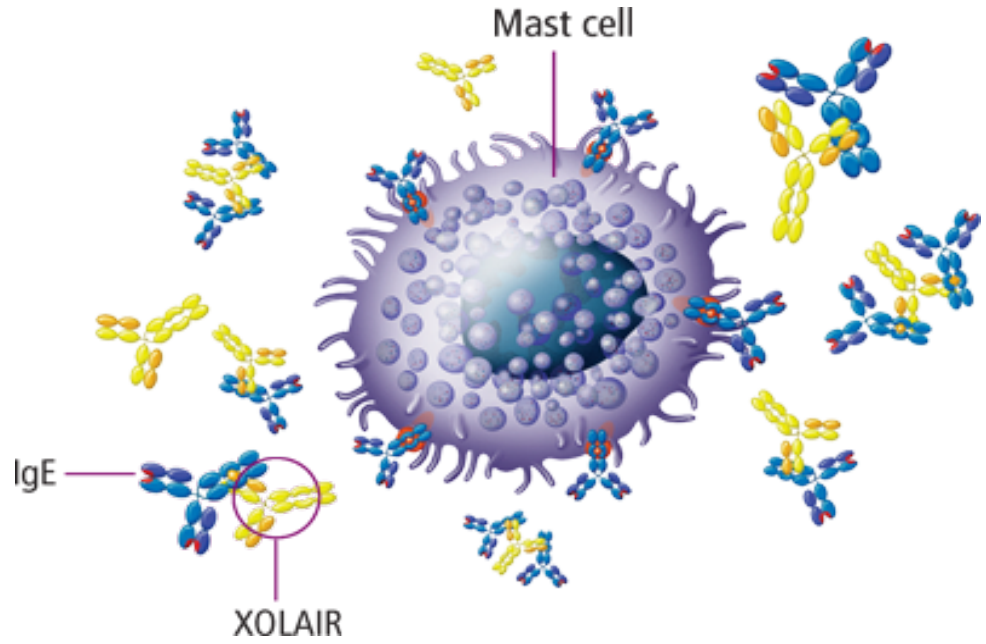


Biologics

Wide range of products that are not synthesized like most drugs where structure is known, could be variable in composition but generally isolated from natural sources.

Cutting Edge

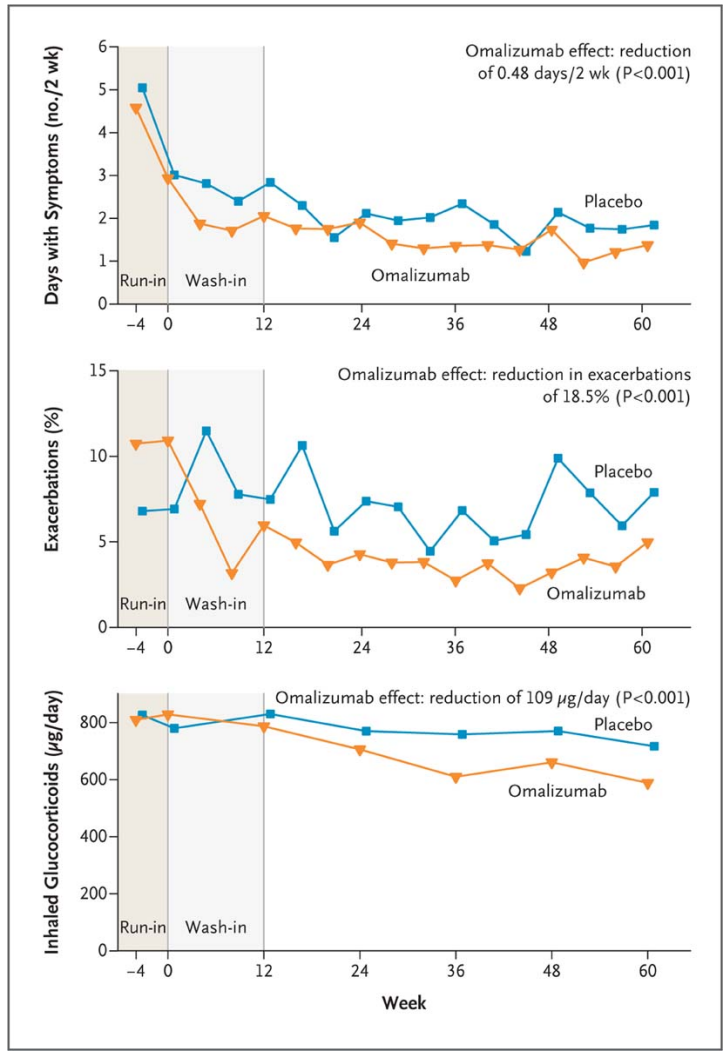
Omalizumab



- Inhibits IgE mediated mediator release
- Reduces allergen presentation
- Decreases asthma exacerbations, hospital admits, ED visits, unscheduled MD visits and rescue therapy, ICS dose, symptoms scores, QOL, time to first exacerbation
- Step 5/6 in 12 and above
- Now approved 6 and older

Number of Days with Symptoms in a 2-Week Interval, Frequency of Exacerbations, and Dose of Inhaled Glucocorticoids over the Course of the Study.

- 419 participants
- RDBPC trial
- 60 weeks
- Primary Outcome: asthma symptoms
- Secondary Outcome: exacerbations
- 60% AA, 40% Latino
- Inner city



Days with Symptoms

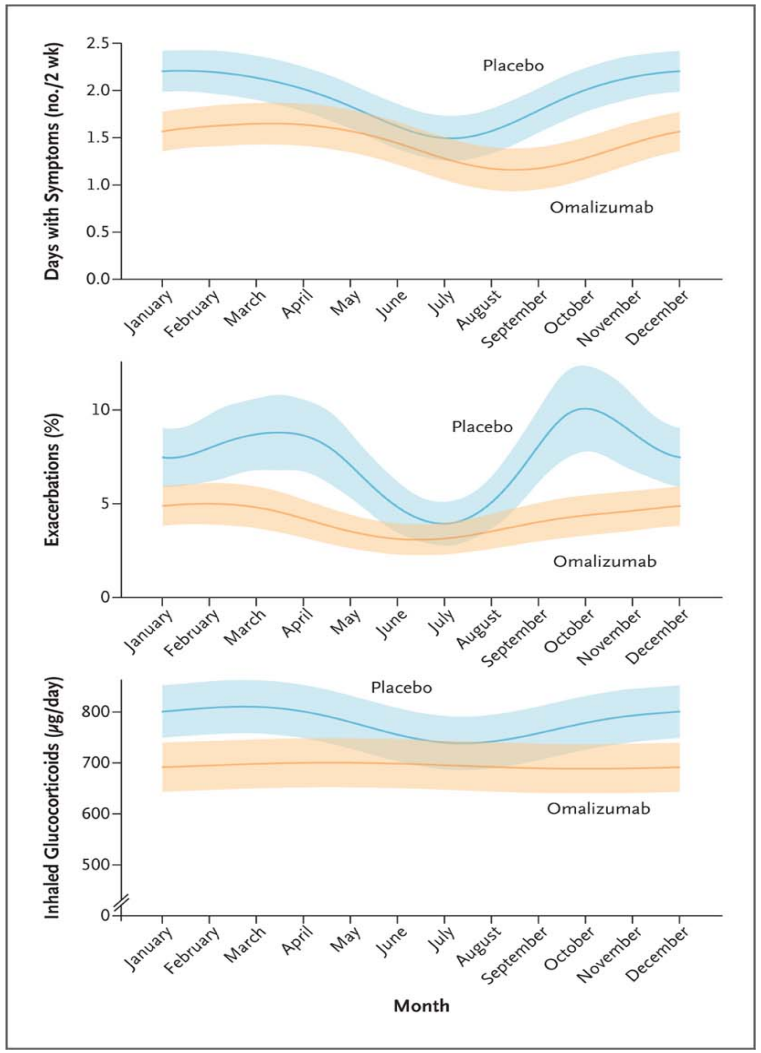
Exacerbations

Inhaled Glucocorticoids

Busse, et al NEJM 2011

The NEW ENGLAND JOURNAL of MEDICINE

Seasonal Variation in Days with Symptoms, Frequency of Exacerbations, and Dose of Inhaled Glucocorticoids on in Days with Symptoms, Frequency of Exacerbations, and Dose of Inhaled Glucocorticoids.



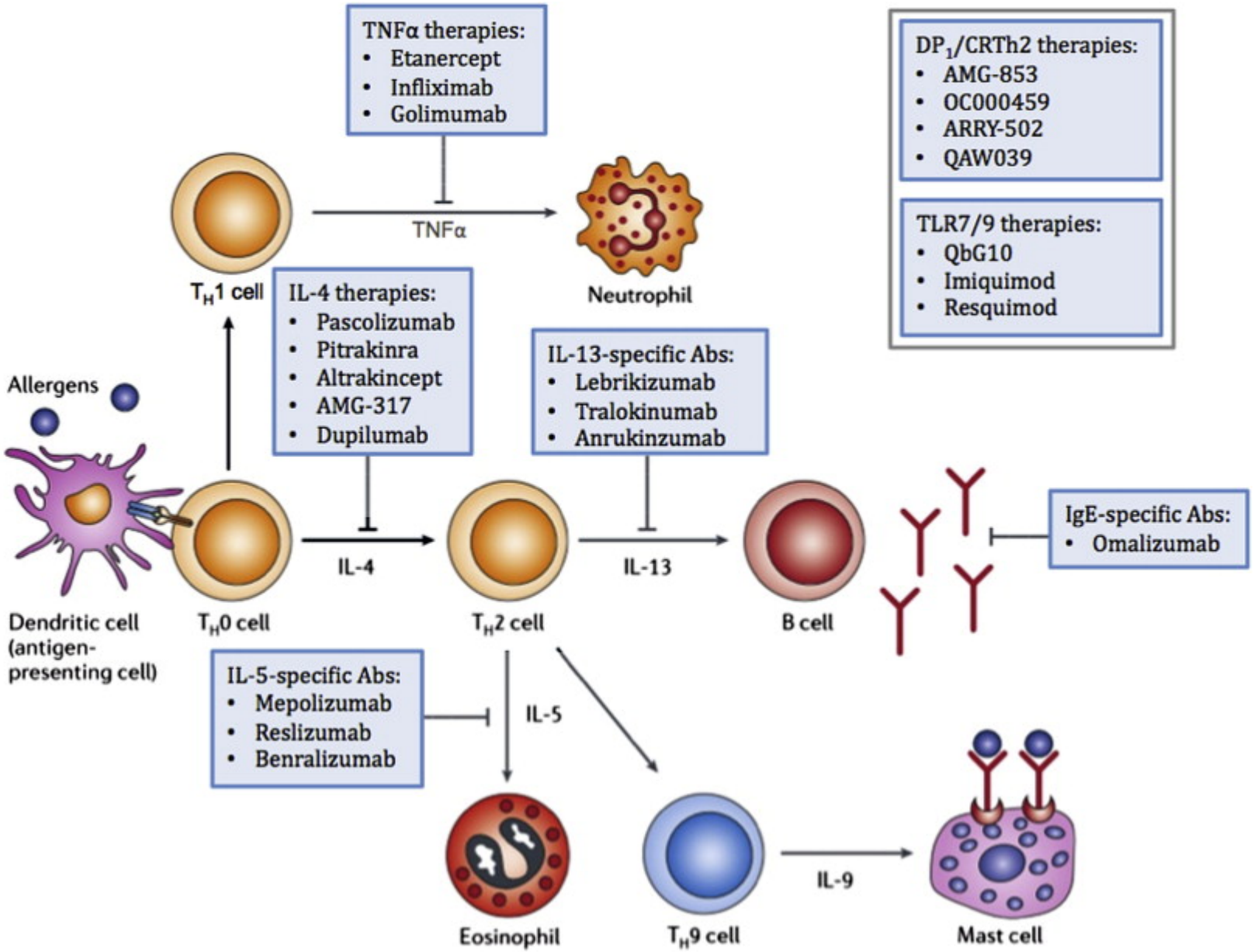
Days with Symptoms

Exacerbations

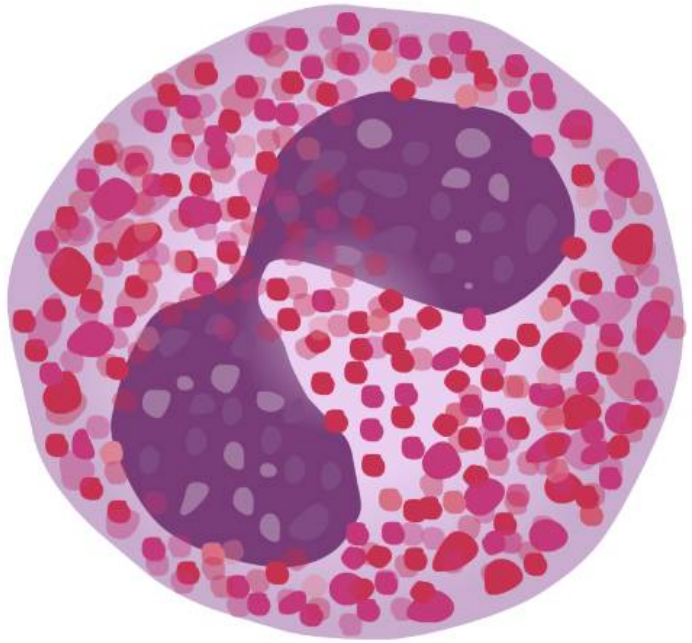
Inhaled Glucocorticoids

Busse, et al NEJM 2011

The NEW ENGLAND JOURNAL of MEDICINE


TNFα therapies:
• Etanercept
• Infliximab
• Golimumab
TNFα
T_H1 cell
Neutrophil
DP_1/CRTh2 therapies:
• AMG-853
• OC000459
• ARRY-502
• QAW039
TLR7/9 therapies:
• QbG10
• Imiquimod
• Resquimod
IL-4 therapies:
• Pascolizumab
• Pitrakinra
• Altrakincept
• AMG-317
• Dupilumab
IL-13-specific Abs:
• Lebrikizumab
• Tralokinumab
• Anrukinzumab
Allergens
IL-4
IL-13
IgE-specific Abs:
• Omalizumab
Dendritic cell (antigen-presenting cell)
T_H0 cell
T_H2 cell
B cell
IL-5-specific Abs:
• Mepolizumab
• Reslizumab
• Benralizumab
IL-5
IL-9
Eosinophil
T_H9 cell
Mast cell

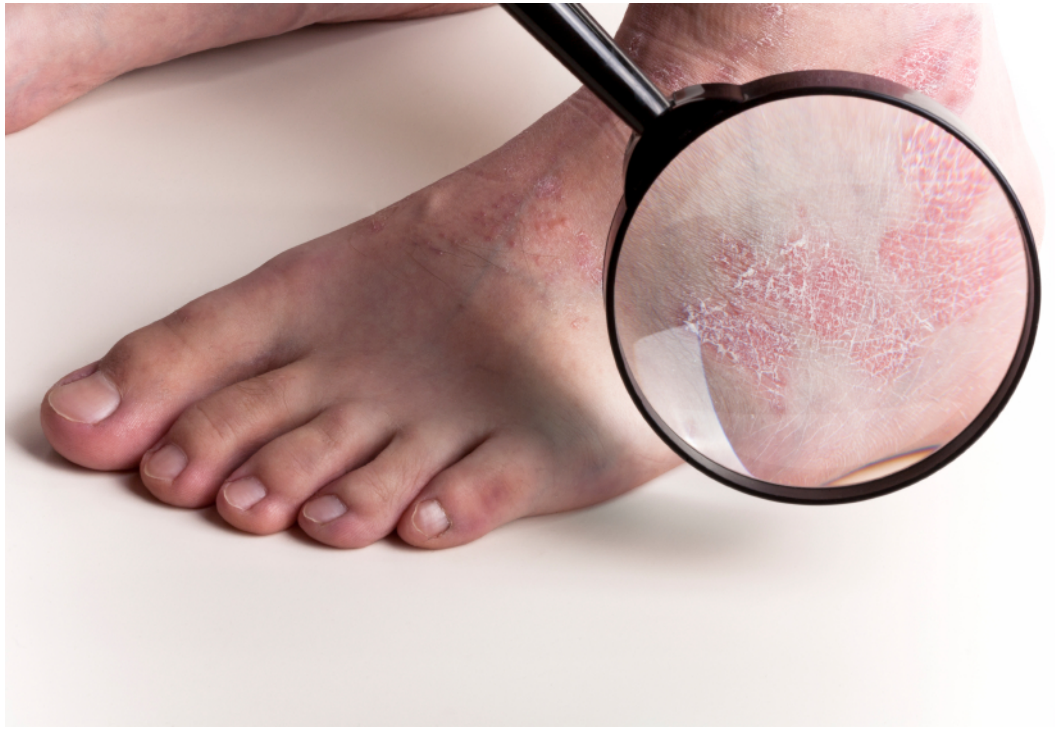
Eosinophil Targets



- IL-5 monoclonal antibody
  - IL-5 induces maturation, activation and recruitment of eosinophils
  - Mepolizumab: 12 and above, severe, persistent asthma, SQ injection Q4 weeks
    - Decreased hospitalizations, ER visits, exacerbations (no change in FEV1, ACQ)
    - Reduction of OCS
  - Reslizumab: severe, persistent asthma, eoso>400, IV
    - Decreased hospitizalizations, ER visits, exacerbations, FEV1, ACQ

Dupilumab

- Fully human mAB to IL-4 alpha subunit of the receptor of IL-4 and IL-13
- IL-4 pushes to Th2
- Moderate to severe persistent asthma, eosinophilia
- Reduced exacerbations, symptoms, improved FEV1
- Already on the market for atopic dermatitis
- Likely will be a good option for children



My concern for Precision Medicine

- Will this further worsen health disparities?

Conclusion

- Continued work on access to care issues is imperative to the health of our children with asthma
- Collaborative Efforts to increase access to specialty care, novel therapies are just as important as work within the community to decrease communication barriers and bridge silos between all sectors.
- Precision Medicine and new medications are exciting, but we must work to ensure fair access to all and more pediatric studies.
- Intervening in younger children can help prevent future adult sequelae
- Th-1 driven asthma is still a huge issue to address in future studies.

Questions?

Thank you so much!

Table 1. Characteristics of Study Participants at Randomization.*

Characteristic	Placebo (N=211)	Omalizumab (N=208)	P Value
Demographic			
Age — yr	10.8±3.4	10.9±3.6	0.99
Male sex — no. (%)	120 (57)	122 (59)	0.71
Race or ethnic group — no. (%)			0.48
Black	121 (57)	131 (63)	
Hispanic	84 (40)	71 (34)	
Other or mixed	6 (3)	6 (3)	
Caretaker completed high school — no. (%)	160 (76)	143 (71)	0.13
≥1 household member employed — no. (%)	163 (77)	139 (67)	0.02
Annual household income <$15,000 — no. (%)	113 (54)	111 (53)	0.95
Clinical			
Duration of asthma — yr	7.0±3.8	7.5±4.0	0.28
Asthma control†			
C-ACT score in the previous month, age 4 to 11 yr	20.7±3.9	20.5±3.8	0.89
ACT score in the previous month, age 12 yr or older	20.3±3.1	20.3±3.8	0.86
Asthma-related symptoms — no. of days in 2 wk preceding visit‡	3.1±3.6	3.0±3.5	0.96
Wheezing	2.6±3.4	2.5±3.1	0.85
Interference with activity	1.6±2.7	1.5±2.4	0.59
Nighttime sleep disruption	0.84±1.96	1.03±2.22	0.19
Missed school — no. of days§	0.25±0.63	0.23±0.76	0.34
Lung function			
FEV_1 — % of predicted value	92.2±17.6	92.9±18.7	0.44
FEV_1:FVC ×100	77.6±9.4	77.3±10.0	0.80
Medication — no. (%)¶			
Step level equal to 1 or 2	60 (28)	53 (25)	0.50
Step level equal to 4 to 6	111 (53)	115 (55)	0.58
Asthma-related health care use in previous yr — no. (%)			
≥1 Hospitalization	52 (25)	52 (25)	0.93
≥1 Unscheduled visit	163 (77)	165 (79)	0.60

* Plus–minus values are means ±SD. P values for the comparison of means and percentages were calculated with the use of the Wilcoxon rank-sum test for continuous variables and the chi-square test for categorical variables. FEV_1 denotes forced expiratory volume in one second, and FVC forced vital capacity.
† Scores on the Childhood Asthma Control Test (C-ACT) and the Asthma Control Test (ACT) were measured on scales of 0 to 27 and 5 to 25, respectively. A score of 19 or less on either test indicates that asthma is not well controlled. The minimally important difference for ACT equals 3 points; that for Childhood ACT is not defined.
‡ The number of days with symptoms was calculated as the largest of the following variables during the previous 2 weeks: number of days with wheezing, chest tightness, or cough; number of nights of sleep disturbance; and number of days when activities were affected. This symptom scale ranges from 0 to 14 days per 2-week period.
§ The number of school days missed was available for 339 of the 419 study participants.
¶ Six treatment steps were established, consistent with report 3 of the National Asthma Education and Prevention Program guidelines to standardize prescribing patterns according to levels of asthma severity; these steps are provided in full in the Supplementary Appendix and are summarized here.[3] Steps 1 and 2 apply to mild asthma, step 3 to moderate asthma, and steps 4 through 6 to severe asthma. At step 0, the recommendation is for no asthma-control medication or albuterol as needed; at step 1, budesonide — 180 μg once a day; at step 2, budesonide — 180 μg twice a day; at step 3, budesonide — 360 μg twice a day; at step 4, fluticasone–salmeterol (Advair, GlaxoSmithKline) — 250 μg fluticasone and 50 μg salmeterol twice a day; at step 5, Advair — 250 μg and 50 μg twice a day plus montelukast once a day; and at step 6, Advair — 500 μg and 50 μg twice a day plus montelukast once a day. (The doses for montelukast are 5 mg per day for children ≤14 years of age and 10 mg per day for those ≥15 years of age.)

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Table 2. Adjusted Treatment Effect on Asthma Symptoms and Health Care Use during 48 Weeks of Follow-up.*

Variable	Placebo (N=211)	Omalizumab (N=208)	Difference (95% CI)†	P Value
Asthma-related symptoms — no. of days in 2 wk preceding visit‡	1.96±0.10	1.48±0.10	−0.48 (−0.77 to −0.20)	<0.001
Wheezing	1.76±0.09	1.32±0.09	−0.44 (−0.70 to −0.17)	0.001
Interference with activity	0.98±0.07	0.70±0.07	−0.28 (−0.47 to −0.09)	0.003
Nighttime sleep disruption	0.59±0.05	0.42±0.05	−0.17 (−0.31 to −0.03)	0.02
Missed school — no. of days§	0.25±0.03	0.16±0.03	−0.09 (−0.18 to −0.01)	0.038
Asthma control¶				
C-ACT score in previous month, age 4 to 11 yr	22.2±0.21	23.0±0.21	0.78 (0.21 to 1.35)	0.007
ACT score in previous month, age 12 yr or older	22.3±0.22	22.5±0.22	0.19 (−0.42 to 0.79)	0.54
Lung function				
FEV_1 — % of predicted value	91.7±0.64	92.6±0.60	0.92 (−0.81 to 2.64)	0.30
FEV_1:FVC ×100	77.5±0.38	77.3±0.36	−0.13 (−1.16 to 0.91)	0.81
Medication				
Adherence — %	88.6±1.80	84.6±1.78	−3.96 (−8.95 to 1.02)	0.12
Step level equal to 1 or 2 — %‖	26.7±3.3	43.6±4.0	16.9 (6.6 to 27.1)	0.001
Step level equal to 4 to 6 — %‖	50.8±4.0	31.2±3.5	−19.6 (−30.1 to −9.1)	<0.001
Inhaled glucocorticoids prescribed — μg/day**	771±23.5	663±23.3	−109 (−172 to −45)	<0.001
Long-acting β_2 agonists prescribed — %	65.5±2.47	55.4±2.44	−10.1 (−16.8 to −3.4)	0.003
Asthma-related health care use — %††				
≥1 Hospitalization	6.3±1.8	1.5±0.9	−4.7 (−8.6 to −0.9)	0.02
≥1 Exacerbation‡‡	48.8±3.7	30.3±3.3	−18.5 (−28.2 to −8.8)	<0.001

* Plus–minus values are means ±SE, adjusted for study site, visit, season, dosing, and baseline levels, unless noted otherwise. FEV_1 denotes forced expiratory volume in one second, and FVC forced vital capacity.
† Unrounded values were used to determine the difference between groups.
‡ The number of days with symptoms was calculated as the largest of the following variables during the previous 2 weeks: number of days with wheezing, chest tightness, or cough; number of nights of sleep disturbance; and number of days when activities were affected. This symptom scale ranges from 0 to 14 days per 2-week period.
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‖ Six treatment steps were established, consistent with report 3 of the National Asthma Education and Prevention Program guidelines to standardize prescribing patterns according to levels of asthma severity; these steps are provided in full in the Supplementary Appendix and are summarized here.[3] Steps 1 and 2 apply to mild asthma, step 3 to moderate asthma, and steps 4 through 6 to severe asthma. At step 0, the recommendation is for no asthma-control medication or albuterol as needed; at step 1, budesonide — 180 μg once a day; at step 2, budesonide — 180 μg twice a day; at step 3, budesonide — 360 μg twice a day; at step 4, fluticasone–salmeterol (Advair, GlaxoSmithKline) — 250 μg fluticasone and 50 μg salmeterol twice a day; at step 5, Advair — 250 μg and 50 μg twice a day plus montelukast once a day; and at step 6, Advair — 500 μg and 50 μg twice a day plus montelukast once a day. (The doses for montelukast are 5 mg per day for children ≤14 years of age and 10 mg per day for those ≥15 years of age.)
** The dose of inhaled glucocorticoids was converted to the budesonide-equivalent dose.
†† Asthma-related health care use was adjusted for study site and dosing because of the scarce data for baseline levels.
‡‡ An exacerbation was defined as a prednisone burst (a minimum of 20 mg per day of prednisone, or the equivalent, taken for any 3 of 5 consecutive days) or a hospitalization.

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