

Inner-City Severe Asthma and Anti-IgE



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Disclosures

- **Employment**

- Cincinnati Children's Hospital

- **Financial Interests**

- Consultant: GSK, Regeneron, TEVA, MERCK
- Honoraria: GSK, Regeneron, TEVA, MERCK

- **Organizational Interests**

- ATS, AAP

- **Research Interests**

- NHLBI, Luther Foundation, Verizon Foundation

- **Gifts**

- Nothing to Disclose

- **Other Interests**

- UpToDate Royalties

Epidemiology

Epidemiology

- **Most children with asthma achieve control with low-medium doses of inhaled steroid (ICS; <500mcg/day fluticasone)**
- **5% children have sustained symptoms despite high dose ICS**
 - **Accounts for 50% expenditures**

Definition

- **ATS/ERS revised definition**
 - **Difficult to treat**
 - **Incorrect diagnosis, co-morbidities, or poor adherence**
 - **Severe therapy-resistant**
 - **Severe asthma despite addressing other factors**

Epidemiology

- **These children demonstrate symptoms in early life**
 - **Decreased lung function in early life**
 - **Atopic disease**
 - **Reversible airway obstruction and bronchial hyperresponsiveness**
 - **High FeNO**

Fitzpatrick AM *JACI* 2006;
Bossely CJ *Eur Respir J* 2009

Inner-City Children

- **High exposure to:**
 - **Medical care barriers**
 - **Environmental risk factors**
 - **Social and psychological factors**
- **Successful treatment of inner city asthma in children often requires interventions in multiple domains**

Management

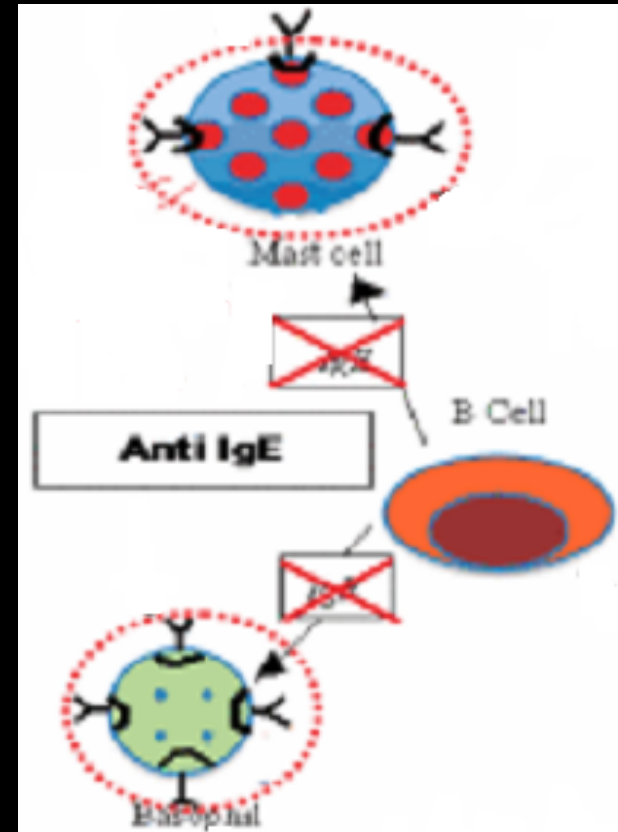
Management

- **Small particle and standard ICS**
- **Oral Corticosteroids**
- **LABA**
- **Antileukotrienes**
- **Methylxanthines**
- **Specific Allergen Immunotherapy**
- **Omalizumab**
- **Emerging: tiotropium, azithromycin, new biologics?**

Omalizumab

Immunomodulation: Omalizumab

- Omalizumab is humanized monoclonal Ab (mAb) to IgE
- Binds free circulating IgE, preventing it from binding to rec.
- First biologic agent approved for clinical treatment of allergic dz.
- In clinical use since 2003

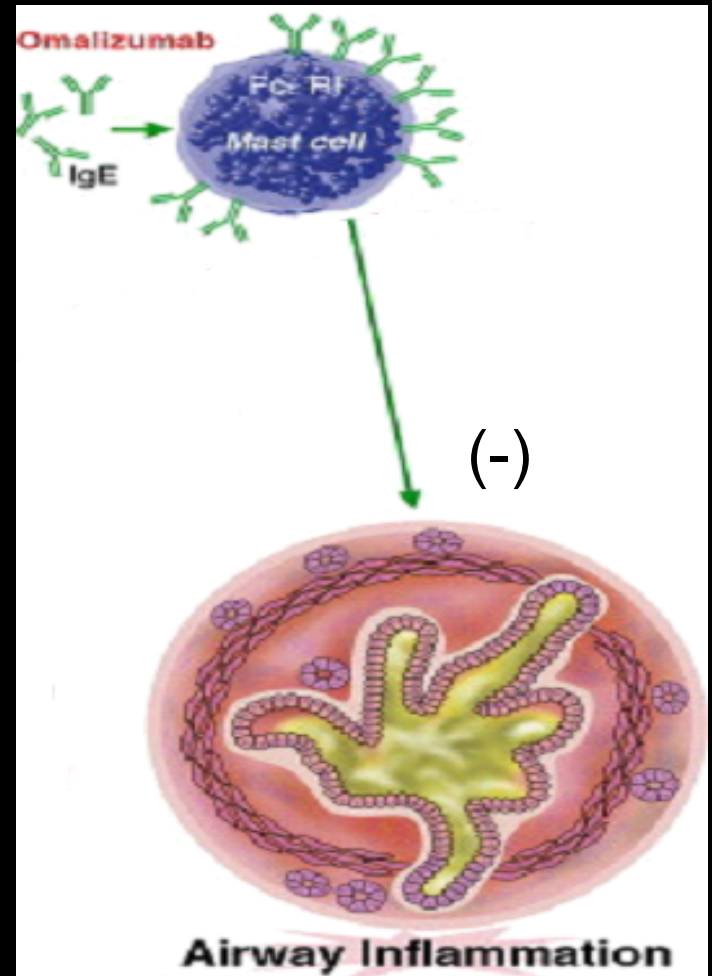


Ballow M. JACI 2006;118:1209-15

Long AA. Allergy Asthma Proc 2009;30:109-19

Clinical Effects

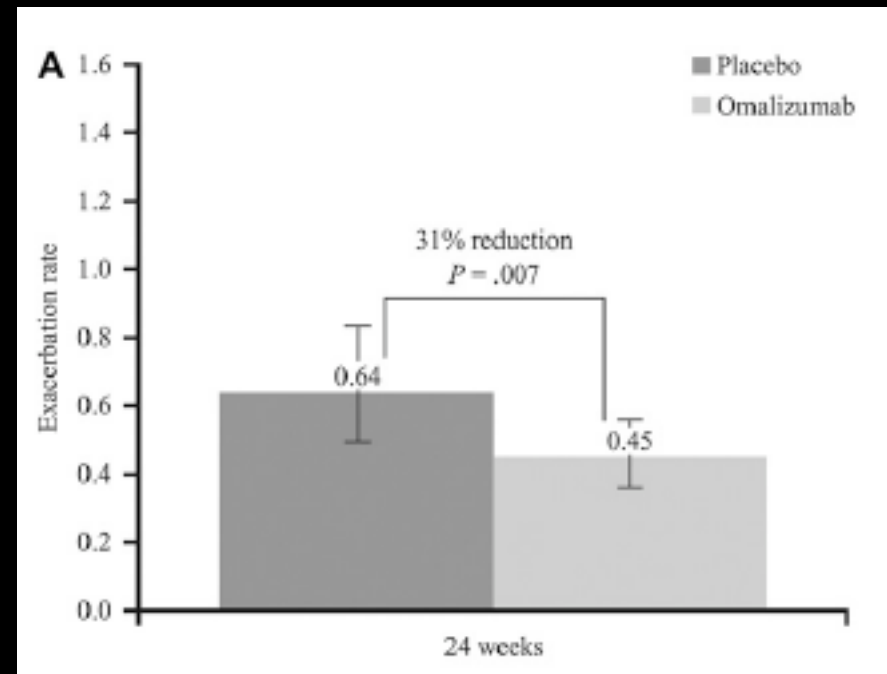
- Early RCT of 525 subjects with severe asthma on daily ICS:
↓ Exacerbations in treatment group
- Observational study of 250 asthmatics receiving ~450 mg q Mo
→ ↓ Daily symptoms by 76%,
→ ↓ Nocturnal symptoms by 84%
→ ↓ Exacerbations by 82%
→ ↓ Hospitalizations by 78%
→ ↑ Asthma related quality of life scores (from 2.9 to 4.5) after 6 mos



Busse W, et al. JACI 2001;108:184-90
Korn S, et al. Respir Med 2009

Immunomodulation: Omalizumab

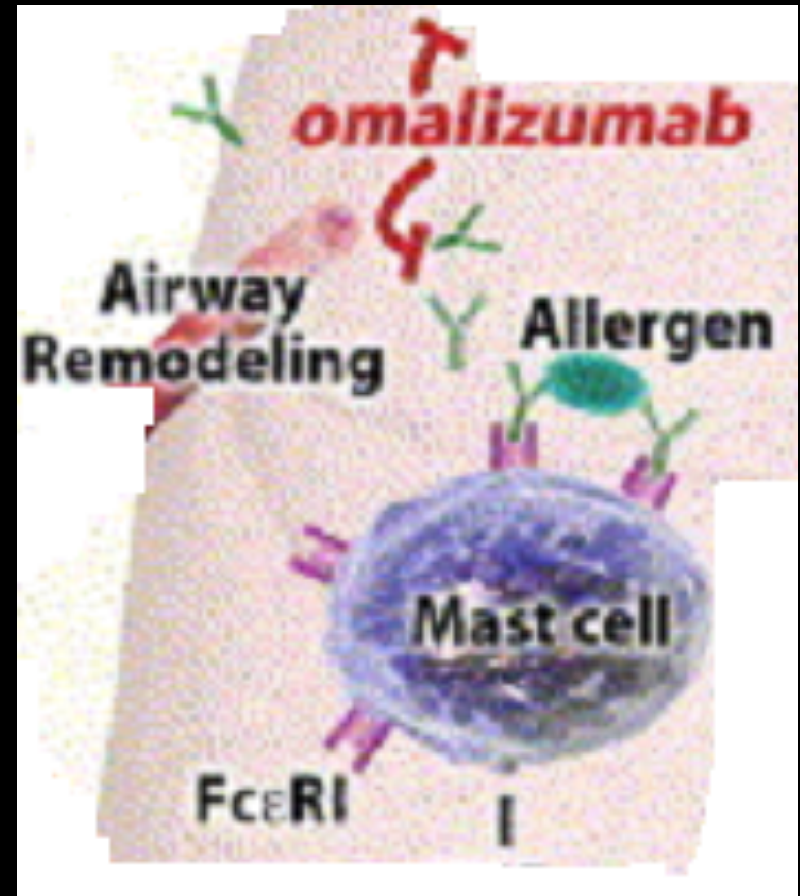
Add-on omalizumab reduced the rate of clinically significant asthma exacerbations in children (6 to <12 years) with uncontrolled moderate-to-severe persistent allergic asthma despite medium to high doses of ICS



Lanier B, J Allergy Clin Immunol. 2009 Dec;124(6):1210-6.

Adverse Reactions

- 0.4% incidence of anaphylaxis (compared to 0.07% in controls)
- Current data do not support
↑ risk of neoplasia or ↓ platelets

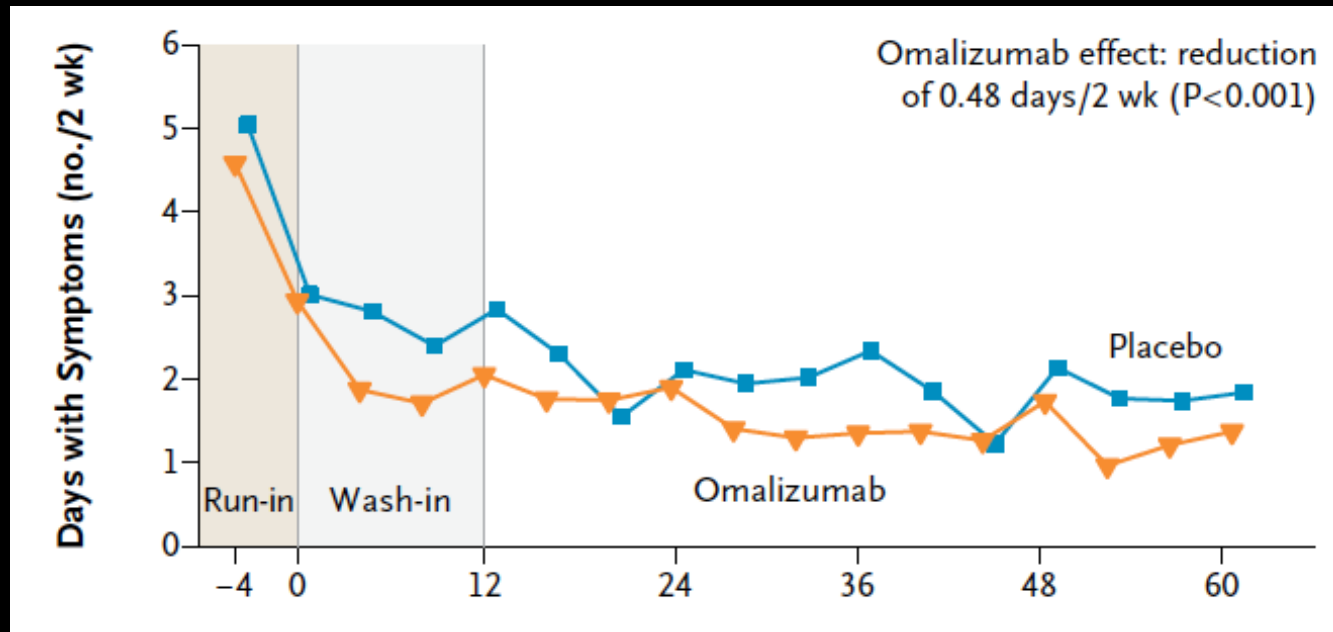


Corren J, et al. Clin Exp Allergy 2009;39:788-97
Ballow M. JACI 2006;118:1209-15

Omalizumab in Inner-City Children

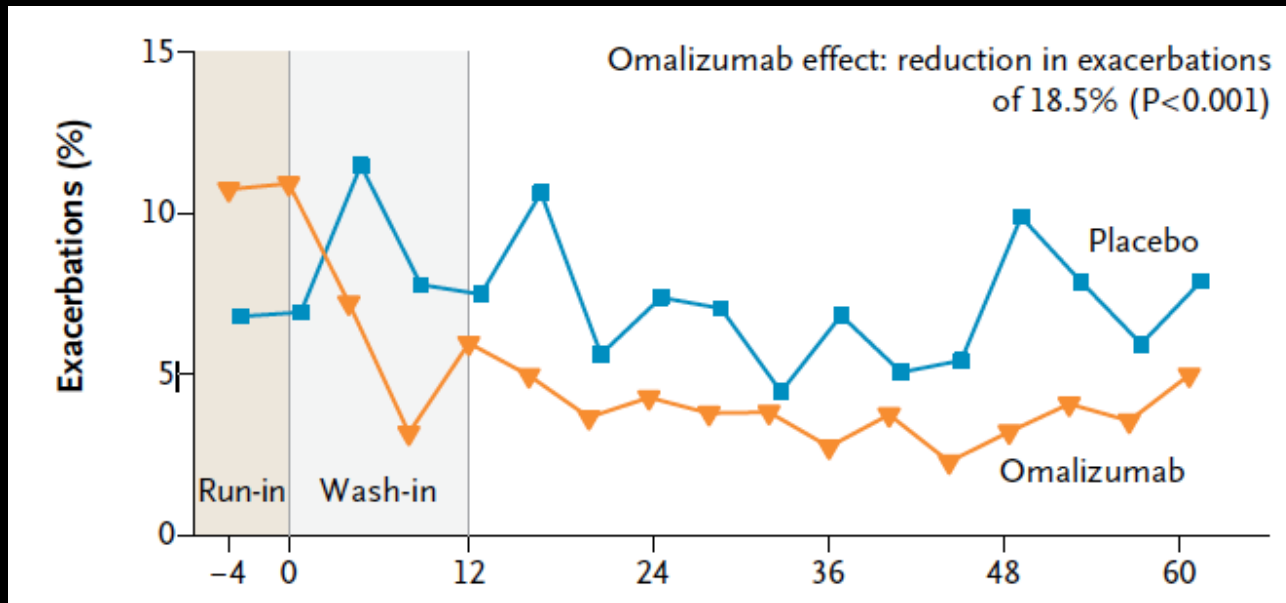
- 419 Inner-city ages 6-20 yrs with moderate-severe persistent asthma in a multi-center RDBPCT by ICAC
- Effectiveness of omalizumab, as compared with placebo, when added to guidelines-based therapy x 60 weeks
- Primary outcome was symptoms of asthma.

Omalizumab in Inner-City Children



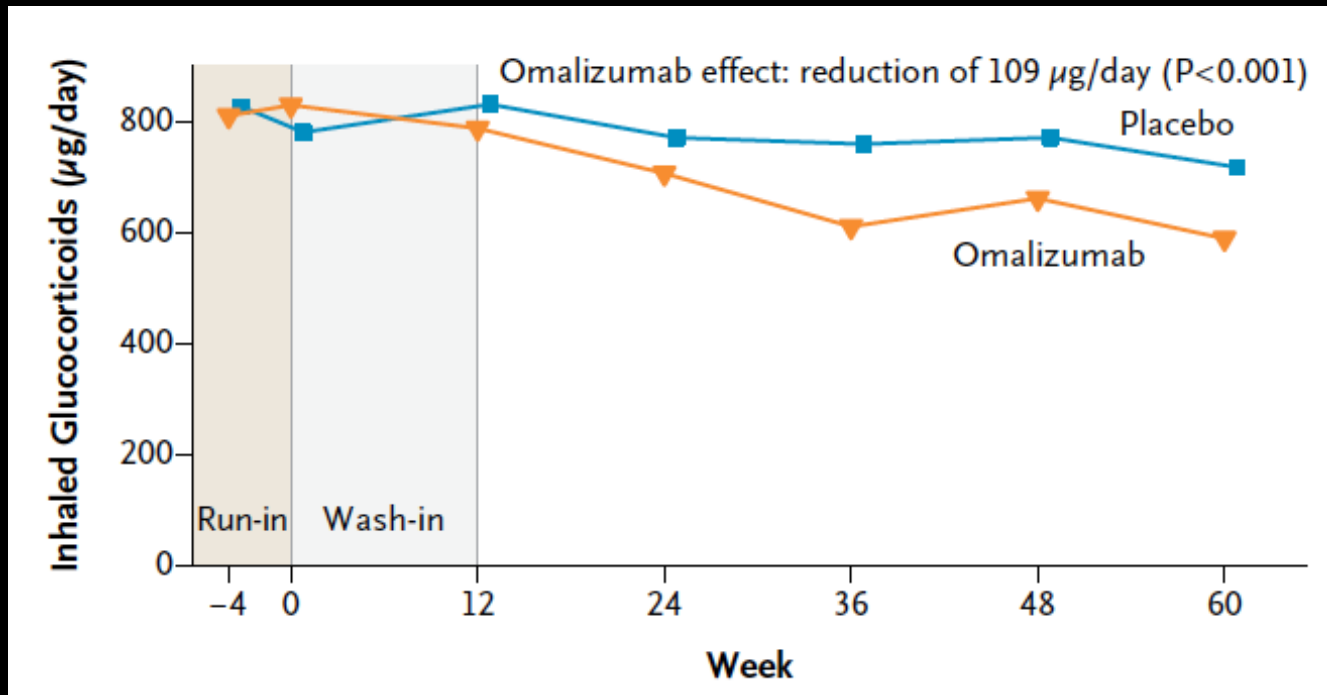
Omalizumab added to guidelines-based therapy for inner-city children improved asthma control (\downarrow 24.5%). Lung function didn't change.

Omalizumab in Inner-City Children



Omalizumab added to guidelines-based therapy for inner-city children decreased exacerbations ($\downarrow 37.9\%$). Greater reductions seen in children sensitized and exposed to cockroach allergen

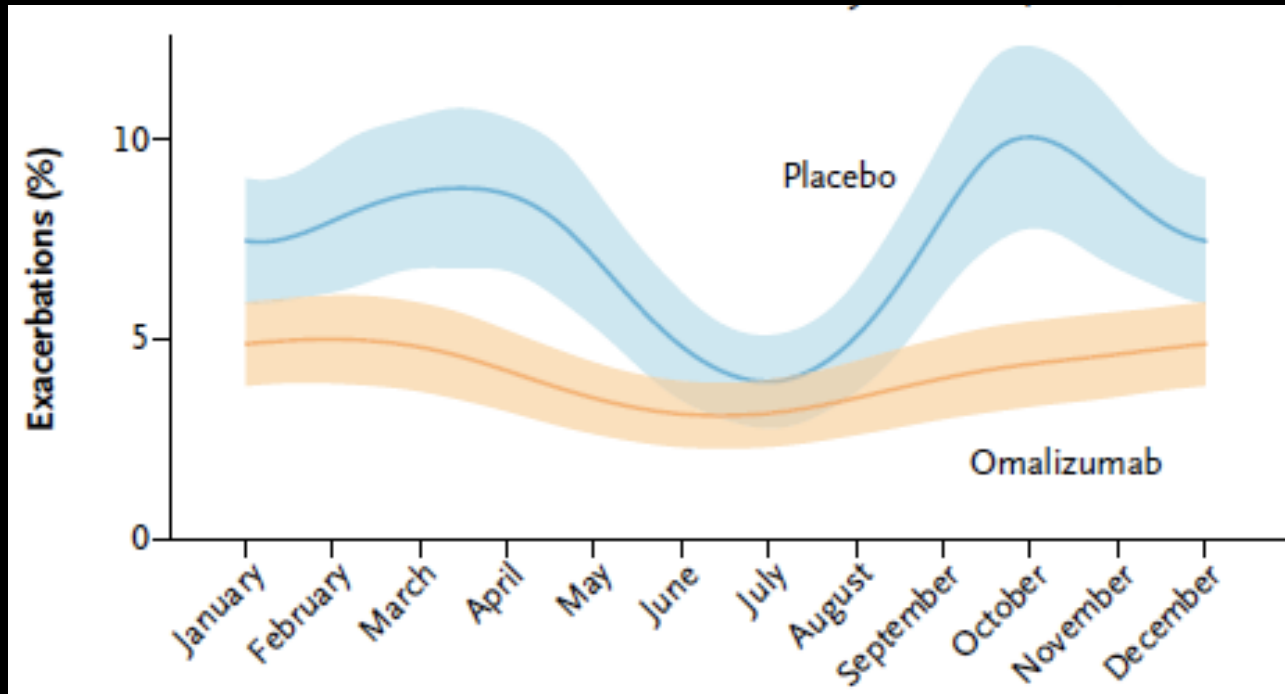
Omalizumab in Inner-City Children



Improved asthma control with omalizumab was achieved with significantly lower doses of inhaled glucocorticoids ($p < 0.001$) and LABA ($p = 0.003$)

Busse WW, N Engl J Med. 2011 Mar 17;364(11):1005-15.

Omalizumab in Inner-City Children



Omalizumab decreased seasonal peaks in exacerbations, post-hoc analysis ($p < 0.001$)

Omalizumab in Clinical Practice

CCHMC Severe Asthma clinic

- **Track population outcomes and discuss cases pre-clinic conference**
- **Multi-disciplinary clinic: Pulmonary, Allergy, SW, adherence specialist, intensive asthma education, coordination with schools, & omalizumab, started June 2014**
- **Systematic workup to assess co-morbidities & airway inflammation**
- **Standardized approach**

Difficult to Treat (DTT) Asthma

- Children with asthma that despite being treated with high dose inhaled steroids (≥ 2 prescriptions) or > 30 days of oral steroids in last year and have 2 of the following:
 - Requirement for second daily controller
 - Urgent care visit for asthma (UC/ED visit or hospitalization)
 - Low lung function

Difficult to Treat (DTT) Asthma

- Prednisone ≥ 3 times in past year
- Low Asthma Control Test (ACT) scores
- Required Xolair (anti-IgE)
- Defined population using electronic algorithms
 - Identification of population ~ 200
 - Tracking of outcomes over time

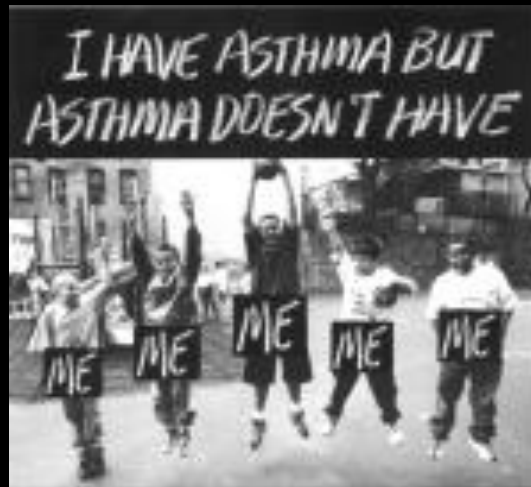
Conclusions

- Omalizumab role in children with high IgE and/or large body habitus unclear
- Unclear best treatment duration or when and how to wean off therapy
- May have a role in children with high healthcare utilization even with h/o poor adherence

Conclusions

- Higher percentage of adolescents with:
 - Neutrophilic or mixed eosinophilic/neutrophilic airway inflammation
 - Vocal cord dysfunction
 - Obesity
 - Challenging to treat
- Still have need for community based interventions as a significant percentage do not come to clinic appointments

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