Morbidity and Co-morbidities for Children with Allergic Rhinitis

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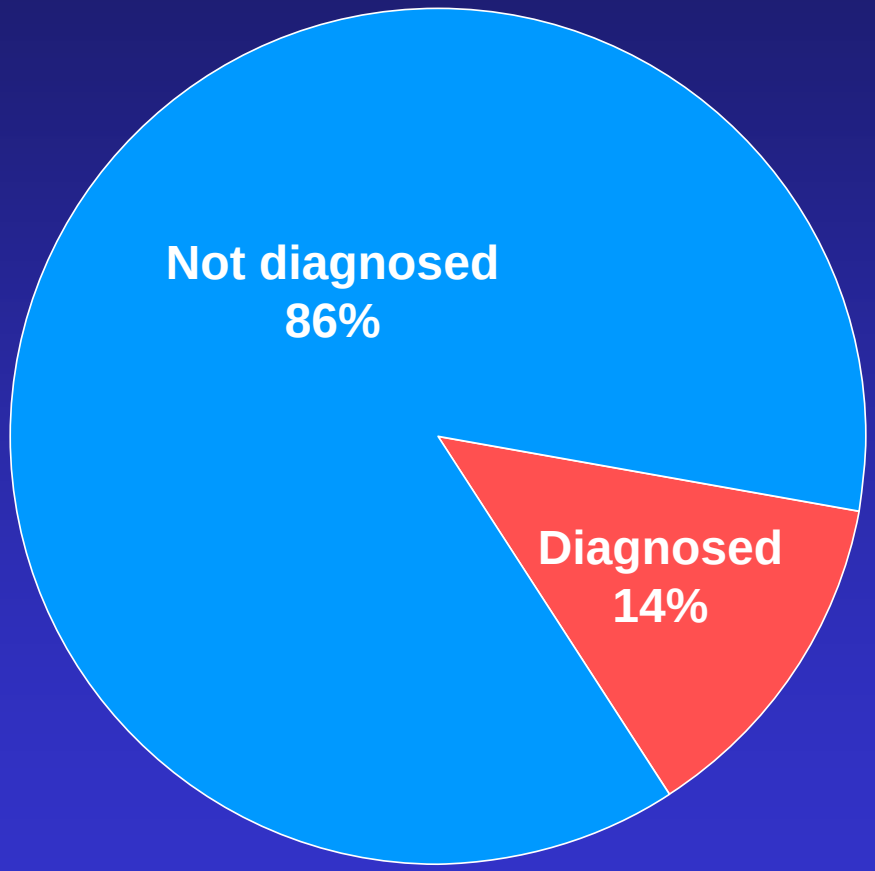
- Abbott
- Alcon
- Amgen
- AstraZeneca
- Boehringer Ingelheim
- Capnia
- Dey
- Genentech
- GlaxoSmithKline
- Meda
- MedImmune
- Merck
- Novartis
- Sanofi
- Schering-Plough
- Sunovion
- Stallergenes
- Teva

High prevalence of allergic rhinitis (AR)

- **AR is the most common of all chronic conditions in children in the USA (Storms,1997)**
- **AR develops before age 20 in 80% of cases**
- **Worldwide prevalence of AR:**
  - **0.8 to 14.9% in the 6–7 year-old age group**
  - **1.4 to 39.7% in the 13–14 year-old age group (ISAAC, 1998)**
- **USA prevalence of AR**
  - **up to 42% for 6-yrs olds (Wright, 1994)**
- **Rising prevalence**
  - **100% increase in each of last 3 decades in developed countries (Linneberg, 2000)**
- **Children frequently lack the ability to verbalize their symptoms**

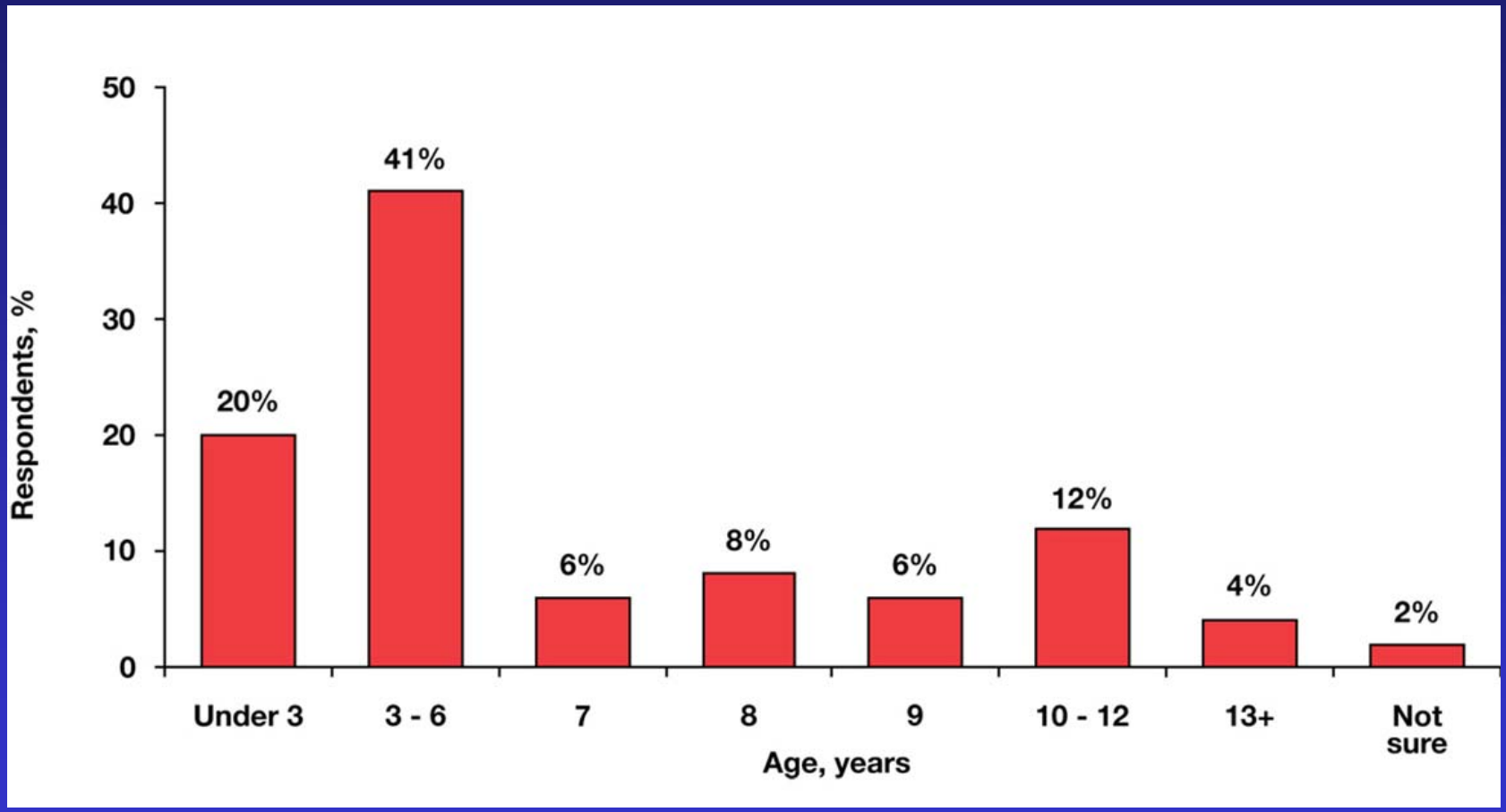
Storms W et al. J Allergy Clin Immunol 1997;99:S820–4; ISAAC. Lancet 1998;351:1225–32; Wright AL et al. Pediatrics 1994;94:895–901. Linneberg A et al. Allergy 2000; 55:767-72

Children Diagnosed with Nasal Allergies: 1 in 7



Meltzer EO, et al. Burden of allergic rhinitis
J Allergy Clin Immunol 2009;124:S43-70

Age at Diagnosis of Children with Allergic Rhinitis



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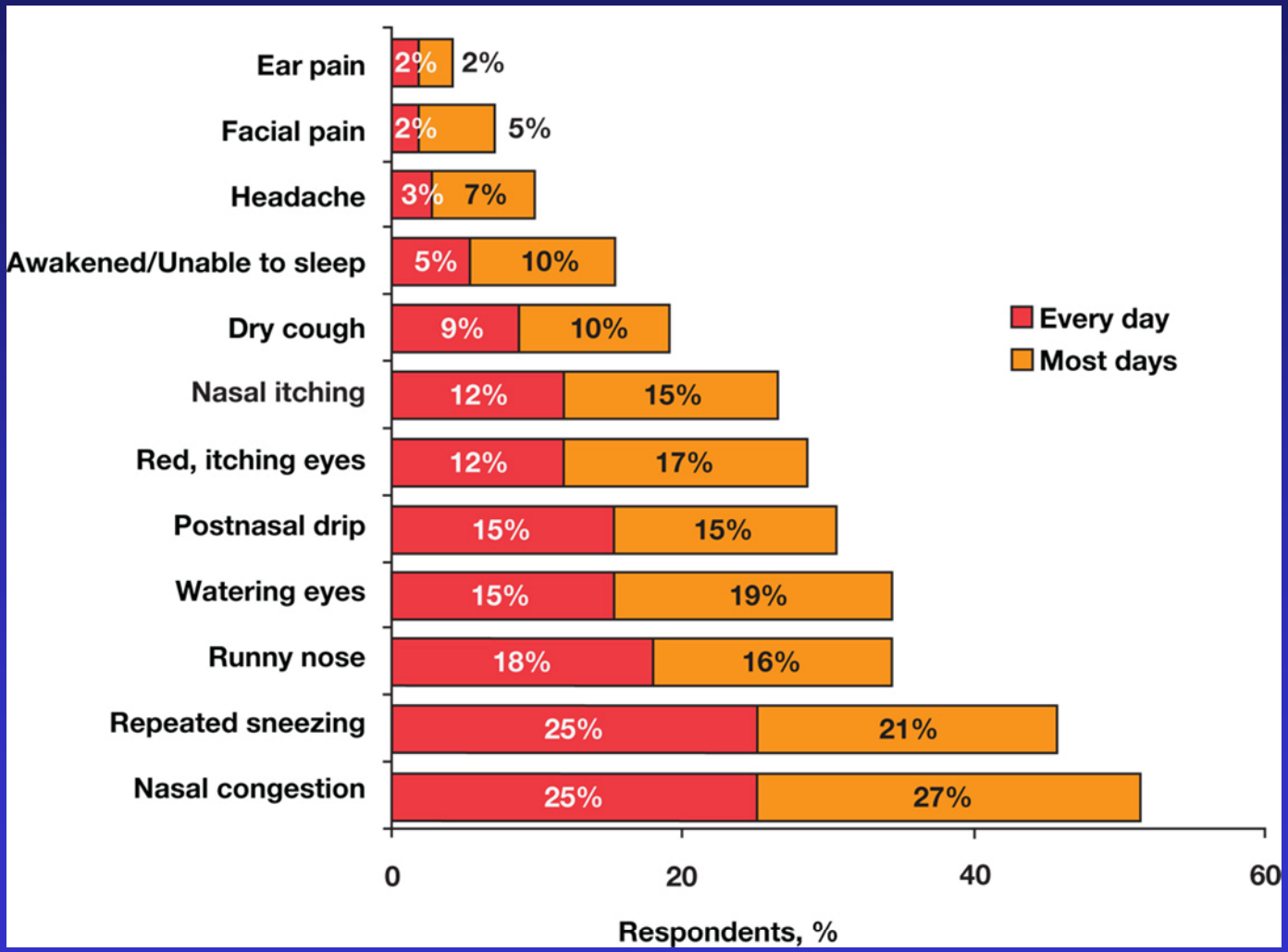
J Allergy Clin Immunol 2009;124:S43-70

Impact on health

- Symptoms and signs of AR
- Co-morbidities associated with AR
  - Conjunctivitis
  - Rhinosinusitis
  - Otitis
  - Dental malocclusions
  - Asthma
- Quality of life with AR

Leynaert B et al. J Allergy Clin Immunol 2000;106:S201–5; Settipane RA. Allergy Asthma Proc 1999;20:209–13; Skoner D et al. Pediatr Asthma Allergy Immunol 1997;11:193–205.

Parent Reports of Children's Nasal Allergy Symptoms During the Worst Month in Past Year



N=500

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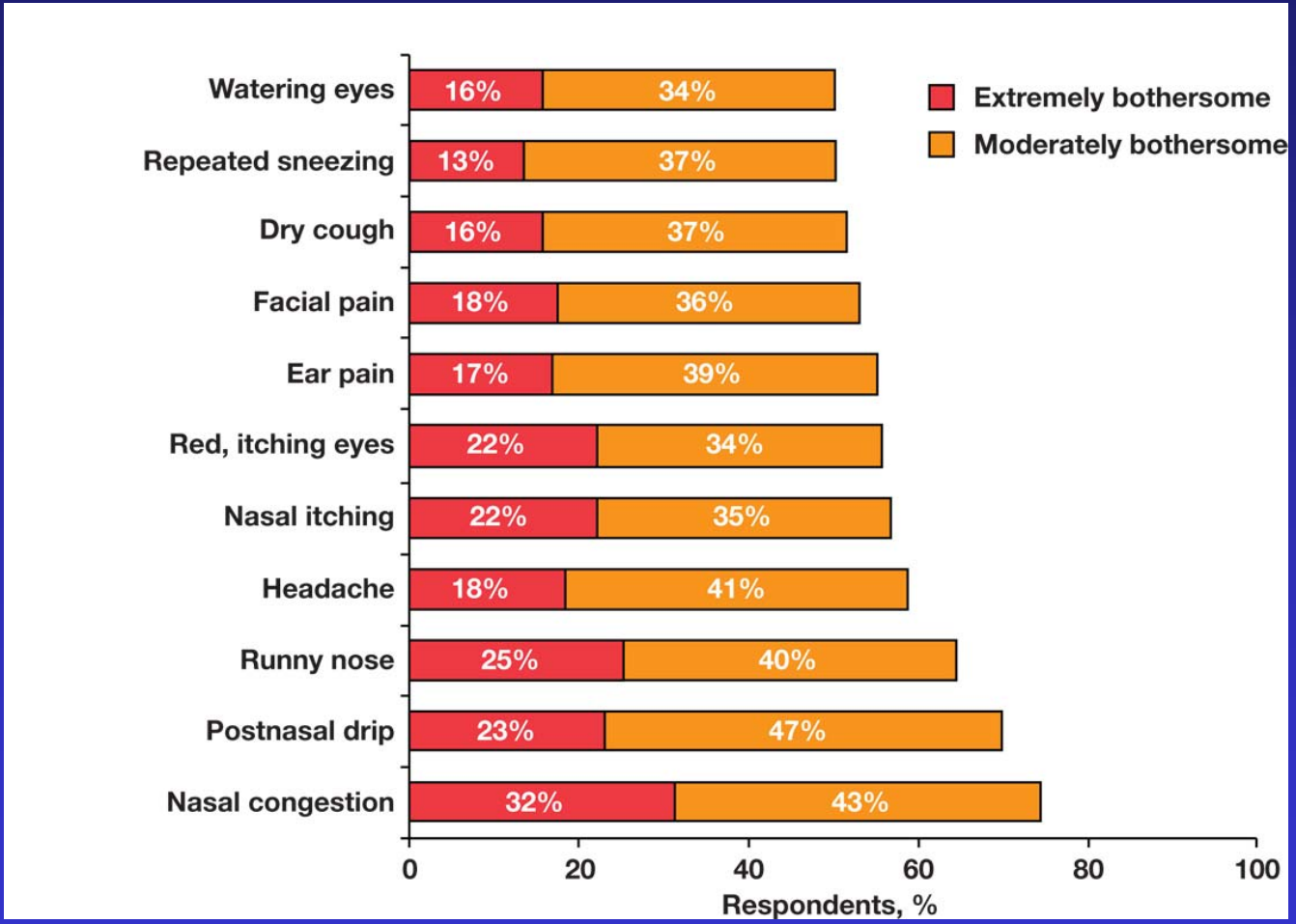
Parent Reports of Severity of Nasal Allergy Symptoms – Extremely or Moderately Bothersome



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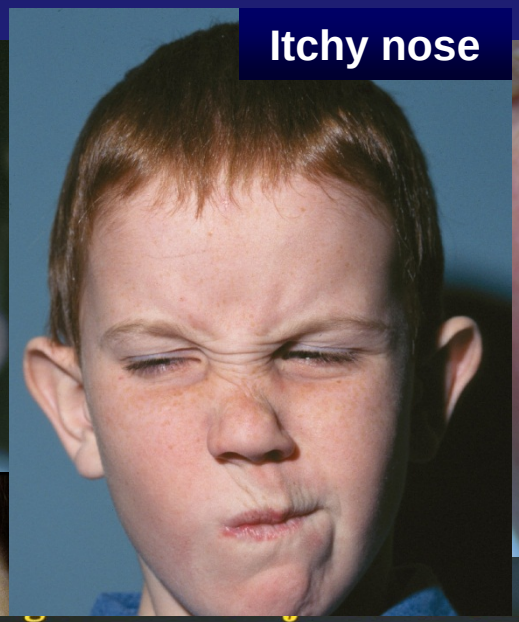
Faces of Allergy

Itchy eyes

Allergic Shiners



Itchy nose

Allergic eyes

Allergic crease

Allergic Salute

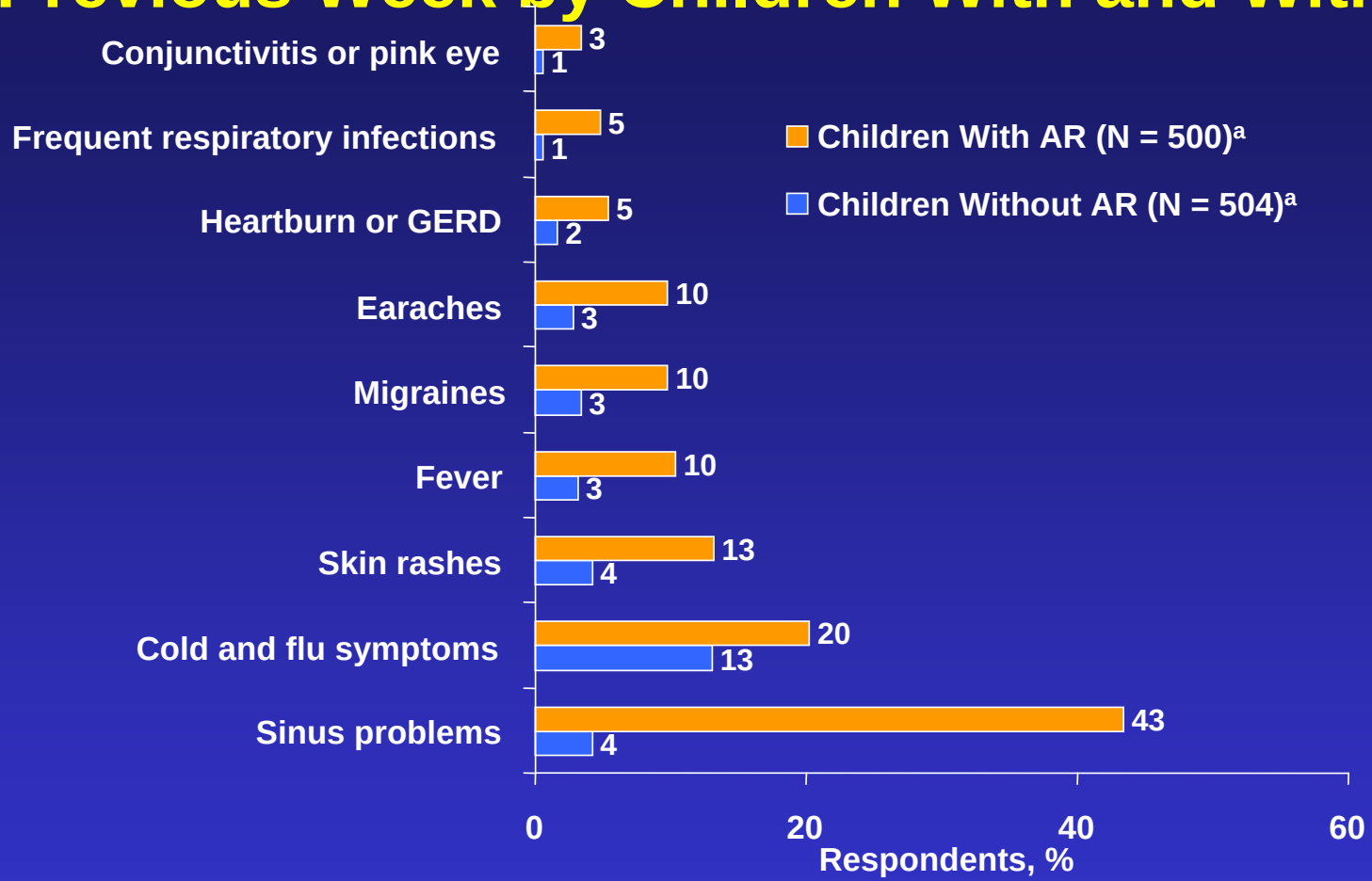
Impact on health

Co-morbidities associated with the disease

- **Conjunctivitis**
- **Rhinosinusitis**
- **Otitis media**
- **Dental malocclusions**
- **Asthma**

Leynaert B et al. J Allergy Clin Immunol 2000;106:S201–5; Settipane RA. Allergy Asthma Proc 1999;20:209–13; Skoner D et al. Pediatr Asthma Allergy Immunol 1997;11:193–205.

Prevalence of Concomitant Conditions Experienced in Previous Week by Children With and Without AR



- Children with AR have a 10-fold increased incidence of sinus problems compared with children without AR
- Children with AR have > 3-fold more skin rashes, fever, migraines, earaches, frequent respiratory infections, and conjunctivitis compared with children without AR

National survey interviewed parents of children 4- 9 years of age and parents and children over 10 years of age . Number of children in the household between 4 -17 years of age diagnosed with AR, nasal allergies, or “hay fever.”
The calculation of overall prevalence of the disease in children was based on all children who were reported by parents to have been diagnosed with nasal allergies of all households .

GERD, gastroesophageal reflux disease.
a. Multiple answers were permitted.

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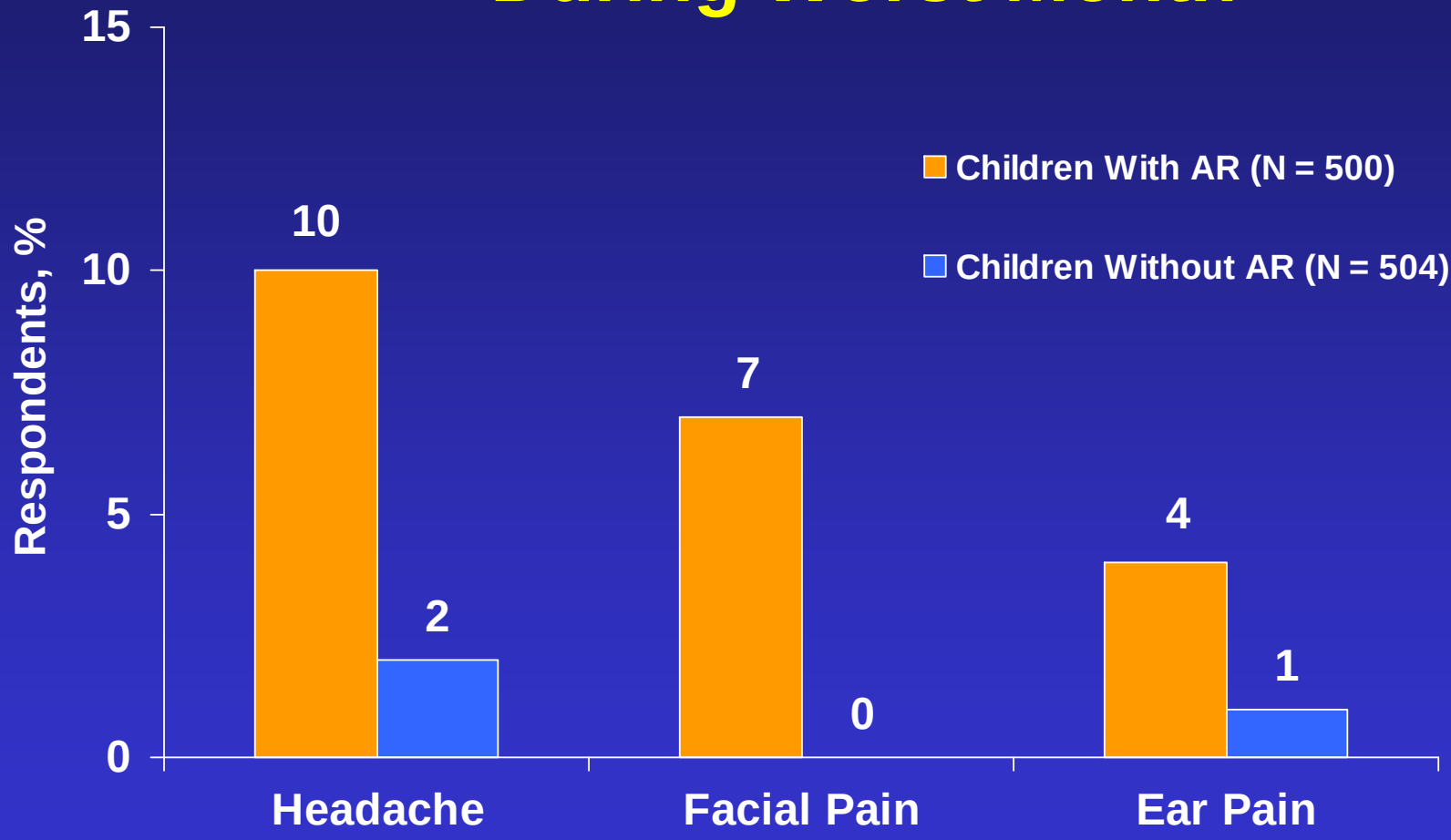
Secondary Symptoms of Nasal Allergies Experienced Most Days/Wk or Every Day During Worst Month



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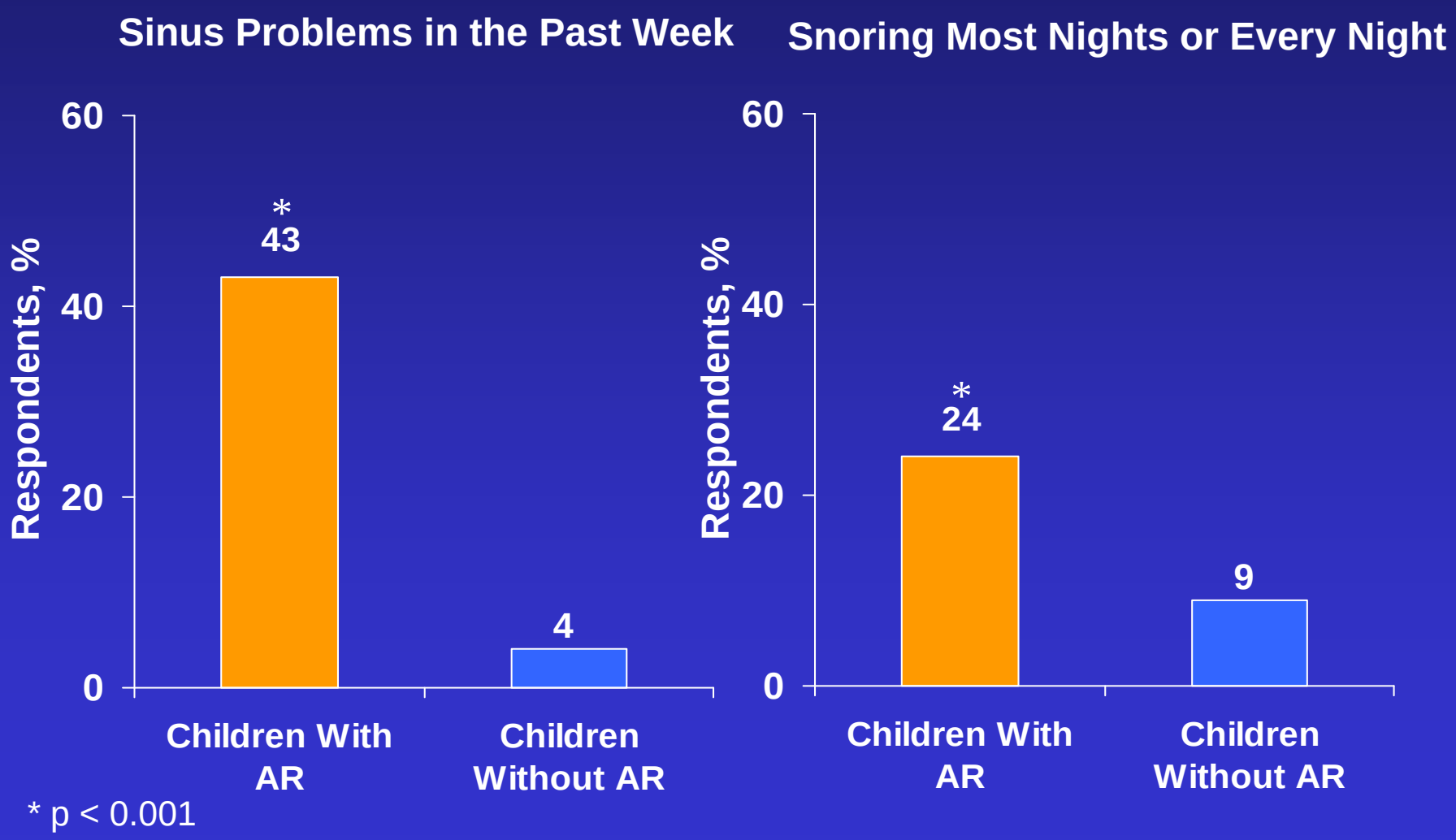
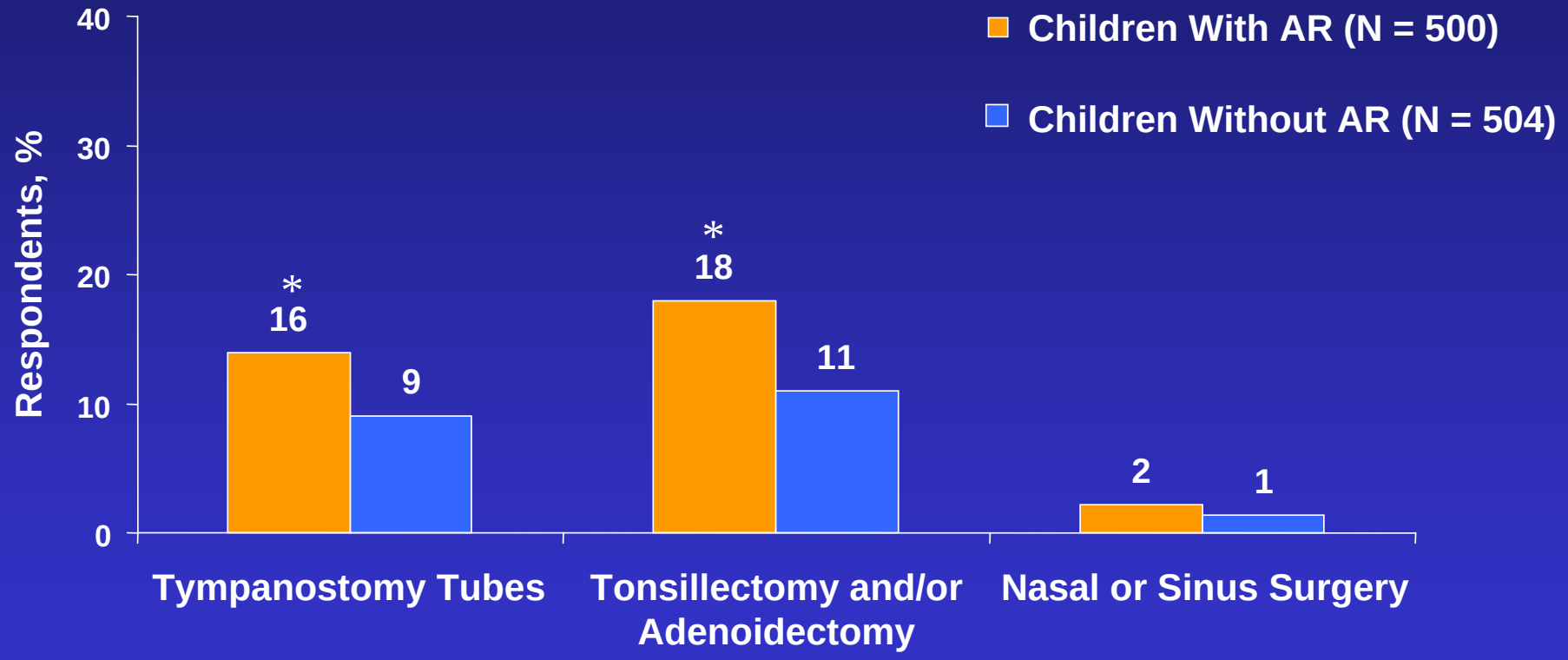
Secondary Symptoms of Nasal Allergies



* p < 0.001

Surgery Potentially Related to AR



* p< 0.05

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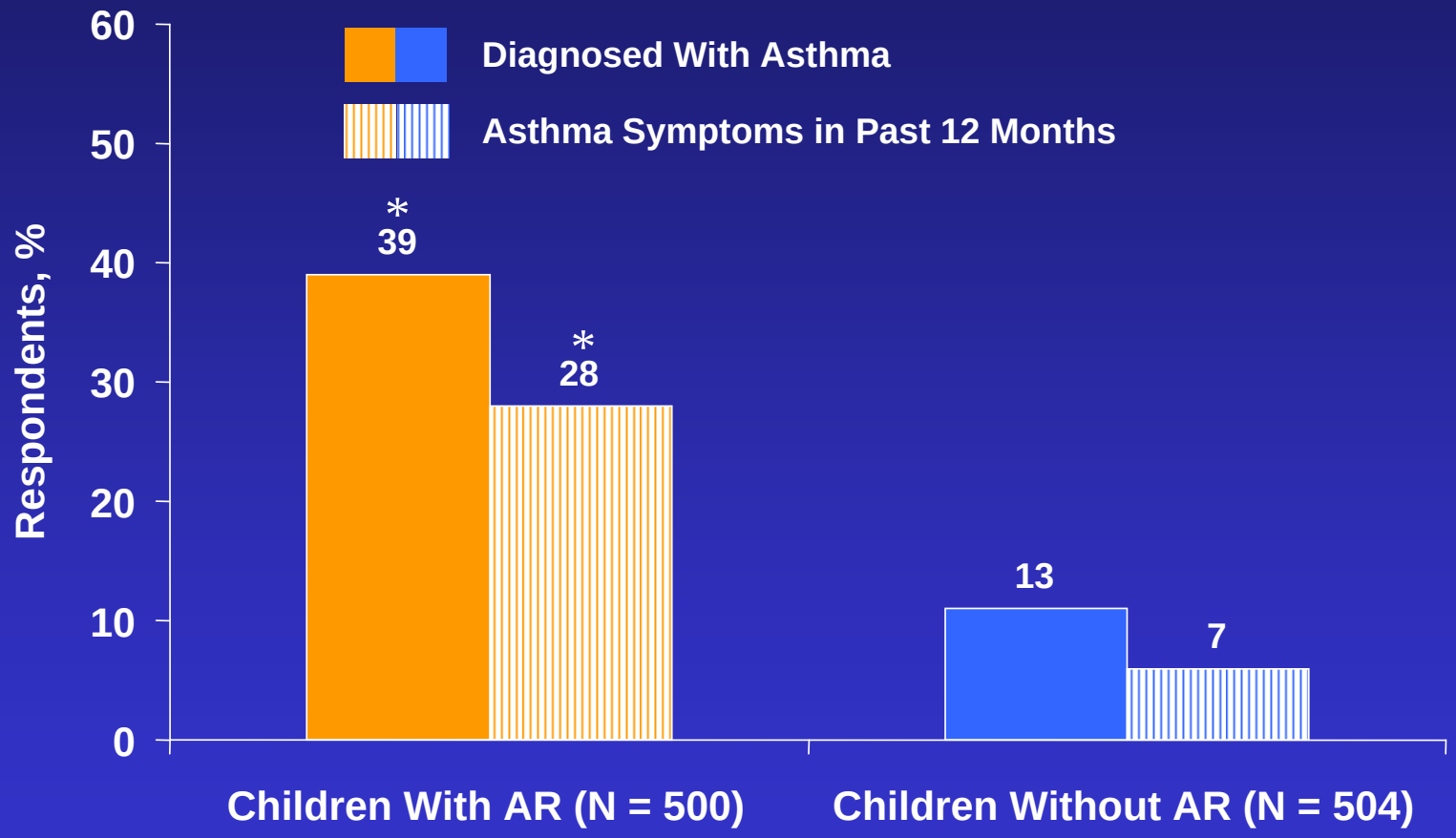
Nasal Allergies Contribute to Other Upper-Airway Problems

	Patients or parents, %		
	AR	**No AR**	Fold difference
Pain or pressure			
Headache*	54	19	2.8
Face*	28	4	7.0
Ear*	24	5	4.9
Surgery			
Tubes placed†	16	9	1.8
Tonsils and/or adenoids removed‡	18	11	1.6
Sinus problems*	43	4	10.8
Snoring*			
Every day	14	5	2.8
Most days	10	4	2.5

AR = Allergic rhinitis.
*$P < 0.001$.
†$P < 0.05$.
‡$P < 0.01$.

Pediatric Allergies in America Survey
Meltzer EO, et al. J Allergy Clin Immunol 2009

Prevalence of Asthma in Children With and Without AR



- Children with AR have a ≥ 3-fold increased incidence of asthma diagnosis and asthma symptoms than children without AR (*p<0.001)

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Impact on quality of life

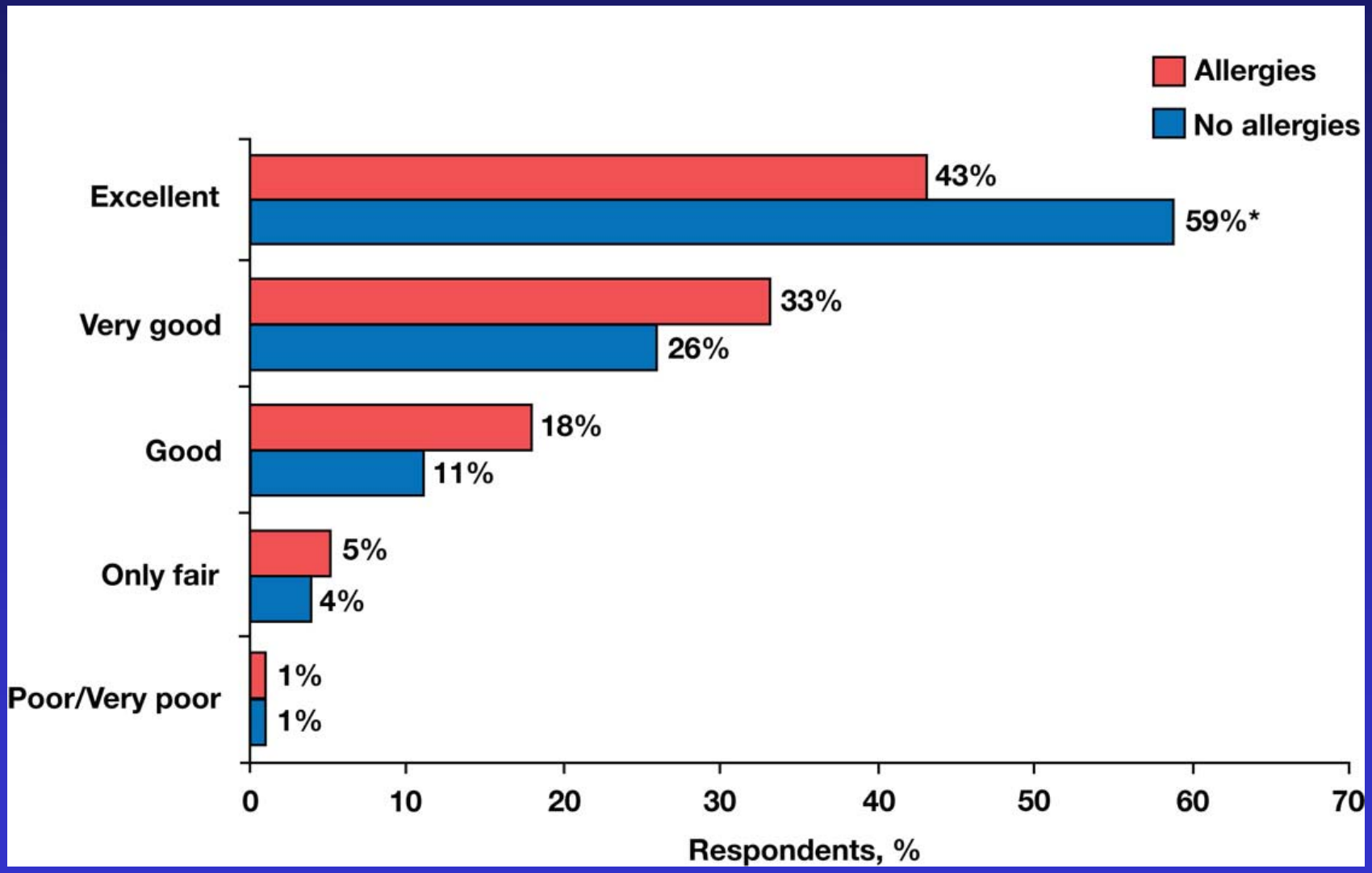
- AR can have a profound impact on the overall and various dimensions of quality of life (QoL) of children

AR has been associated with:

- Sleep disturbances
- Emotional problems
- Activity limitations
- Mental impairments
- Social interruptions
- Practical disruptions

Meltzer EO. J Allergy Clin Immunol 2001;108:S45–53;
Blaiss M. Curr Med Res Opin 2004; 20(12):1937–52.

General Health Comparison by Parents of Children With (n=500) and Without (n=504) Allergic Rhinitis



*P<0.05

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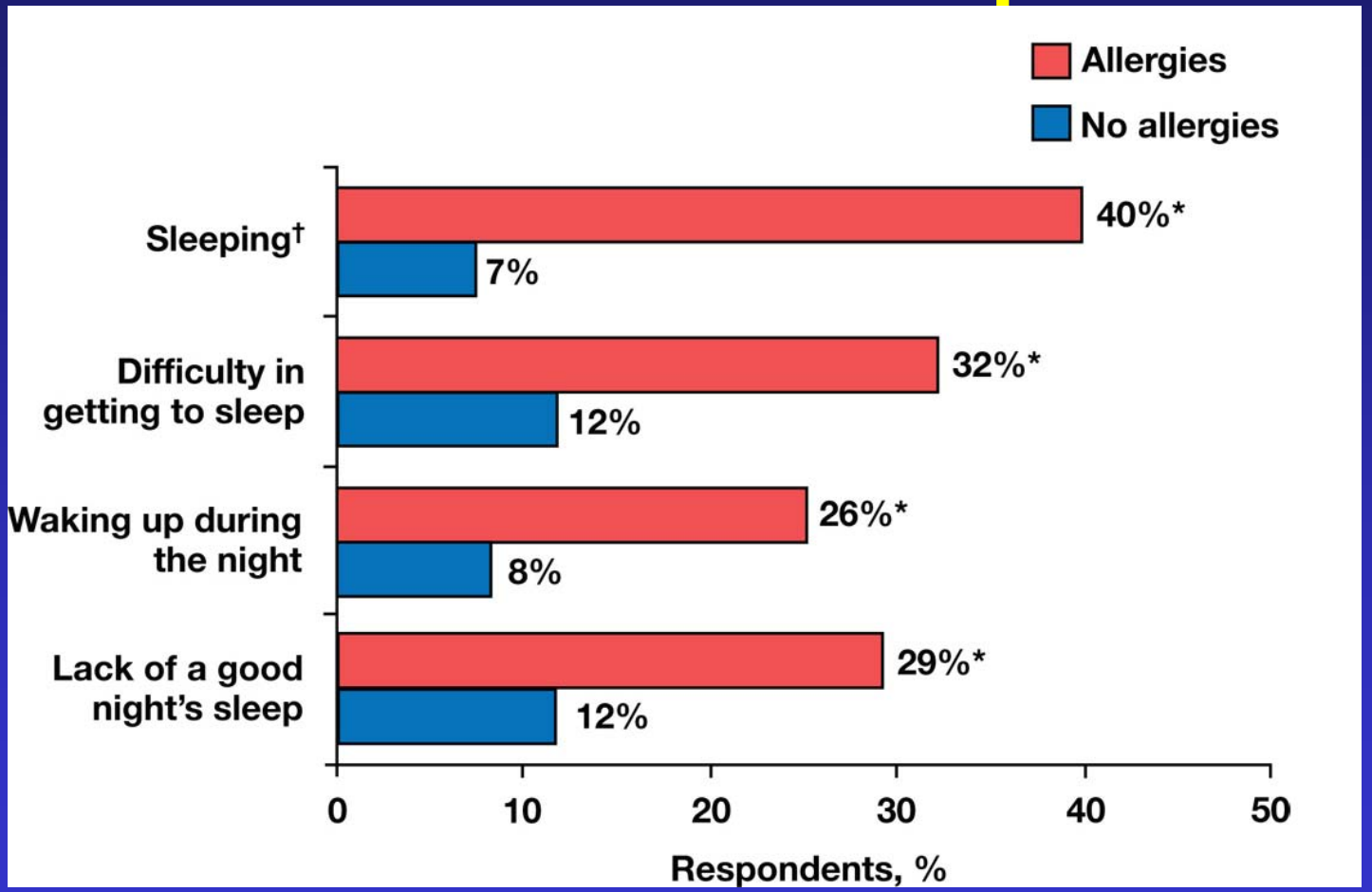
Parent Perceptions on the Effect of Nasal Allergy Symptoms on Children's Sleep



*P<0.05

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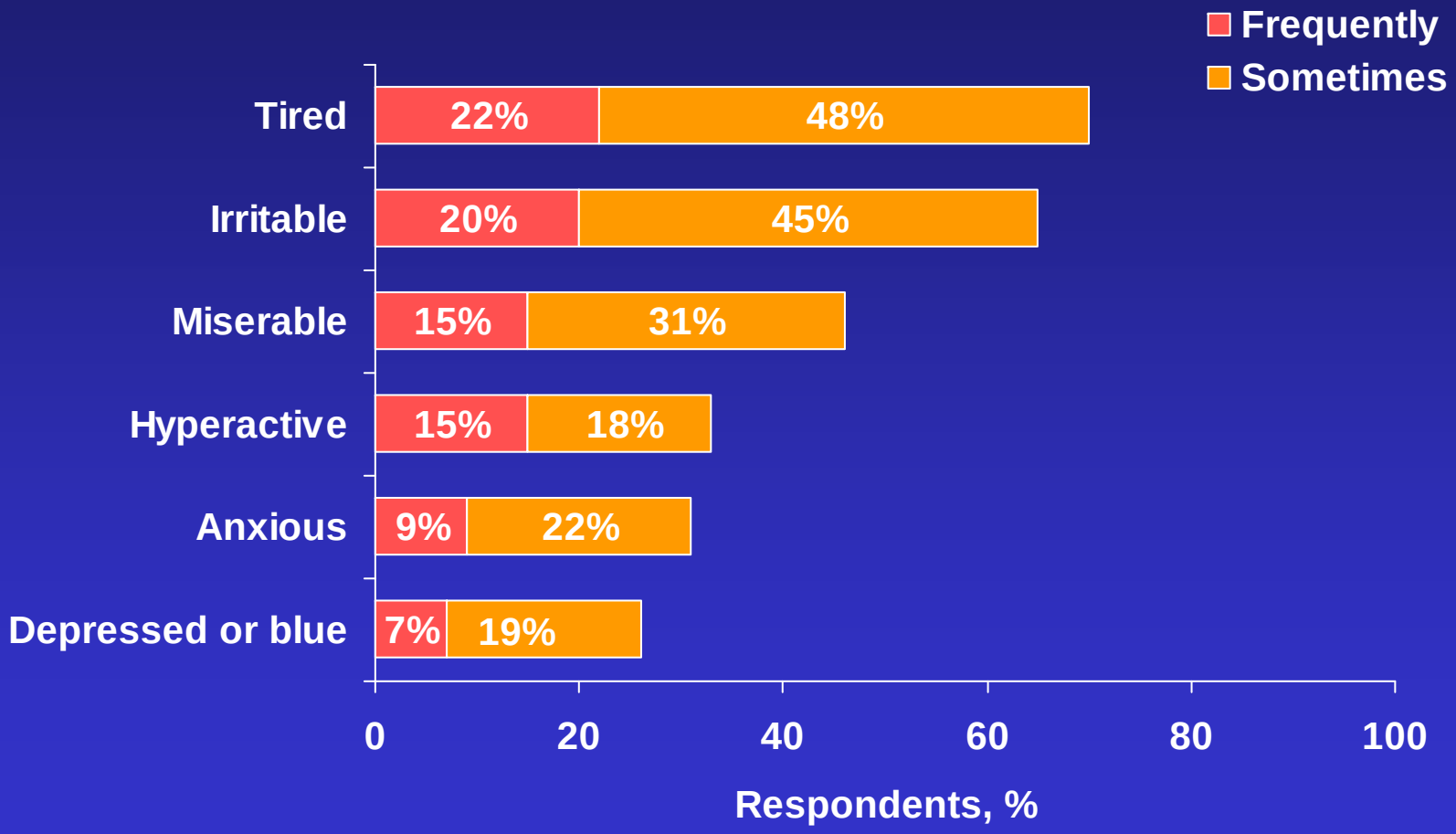
More Than 65% of Children Are Tired and Irritable Because of Allergy Symptoms



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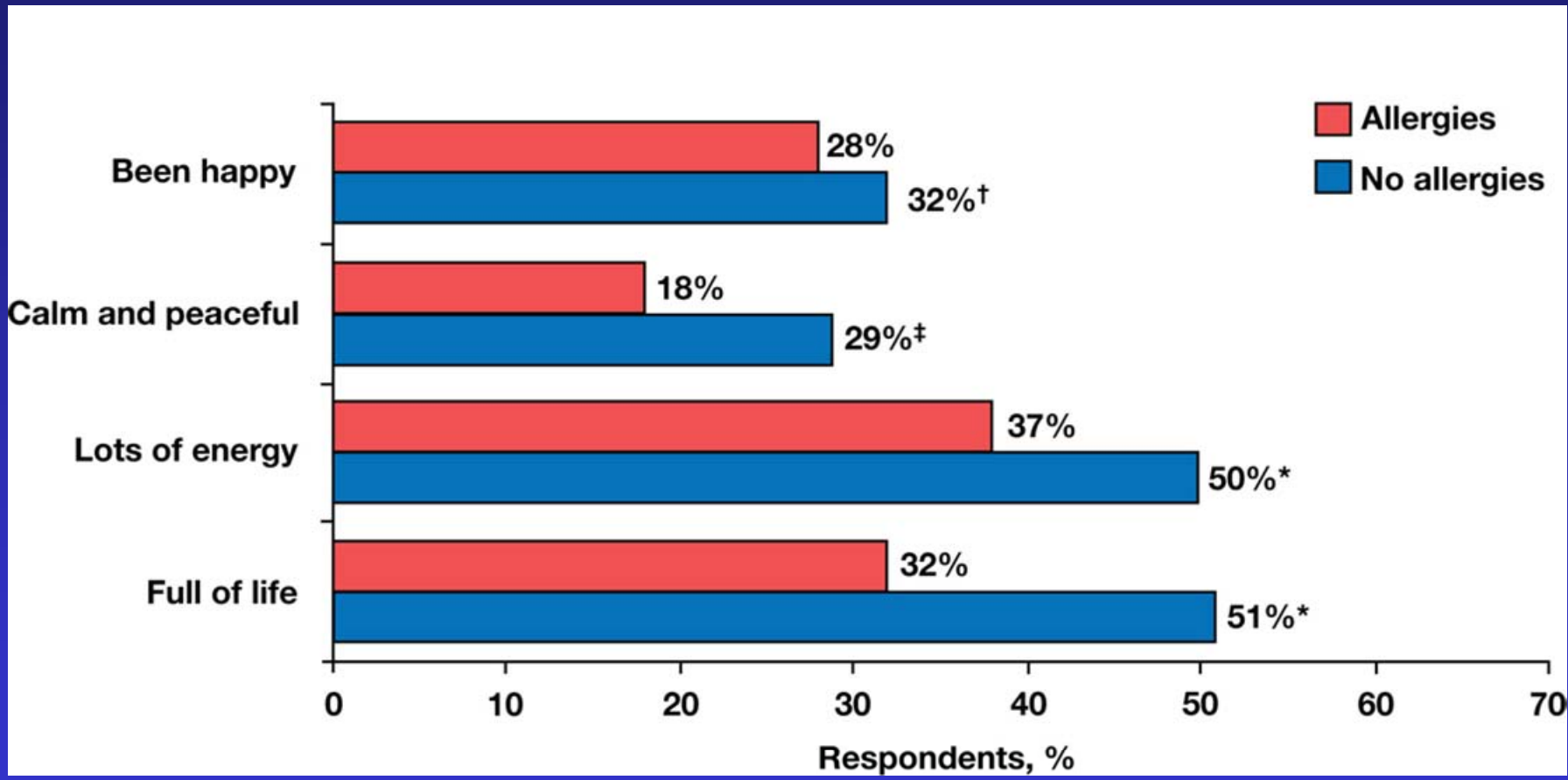
J Allergy Clin Immunol 2009;124:S43-70

Parents Perceptions of Overall Feelings of Well Being in Children With (n=500) and Without (n=504) Allergic Rhinitis



*P<0.05

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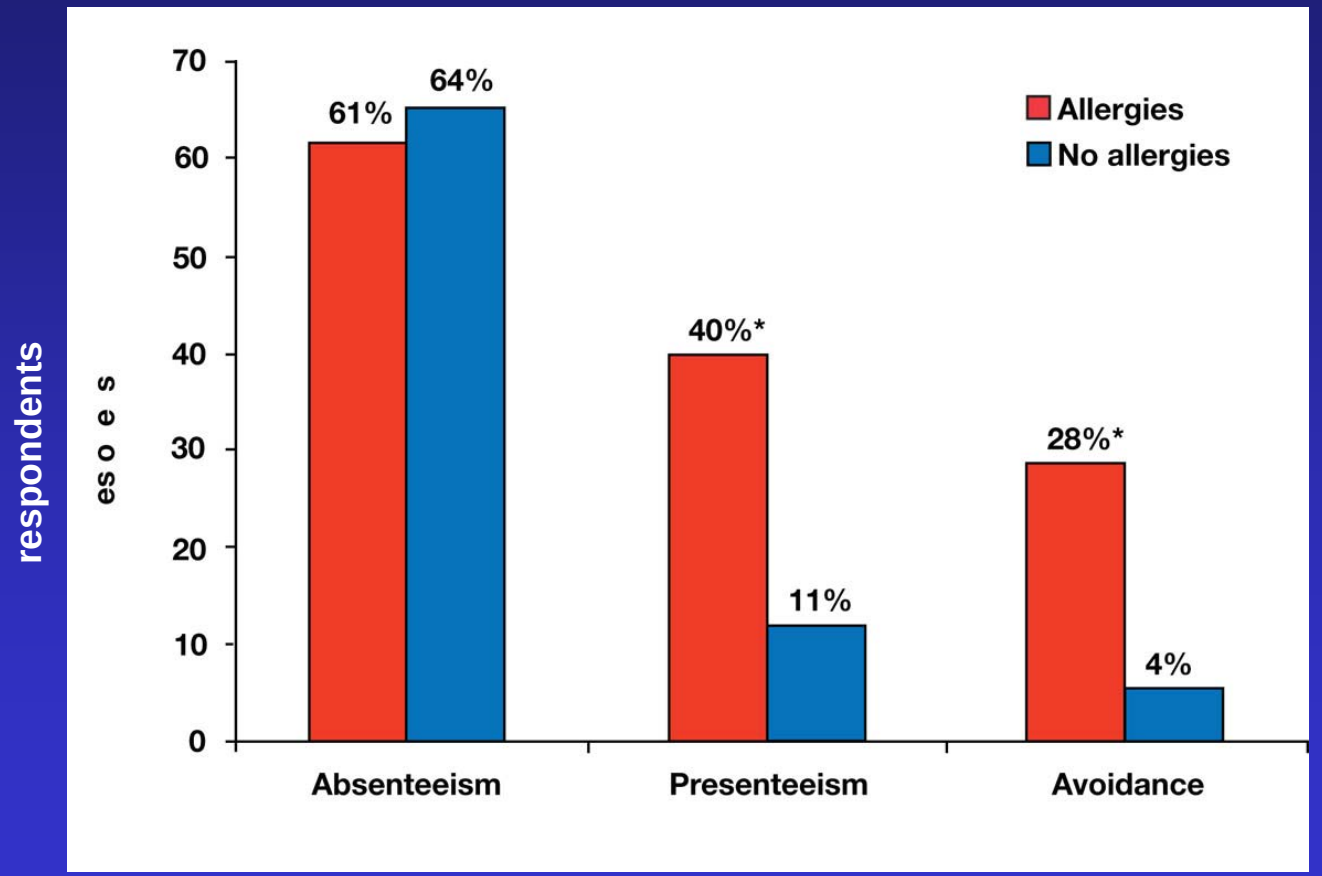
J Allergy Clin Immunol 2009;124:S43-70

Parent Perceptions of Allergy/Health Effects on School Absenteeism and Presenteeism, and Avoidance of Daily Activities in Children With and Without Allergic Rhinitis



*P<0.05

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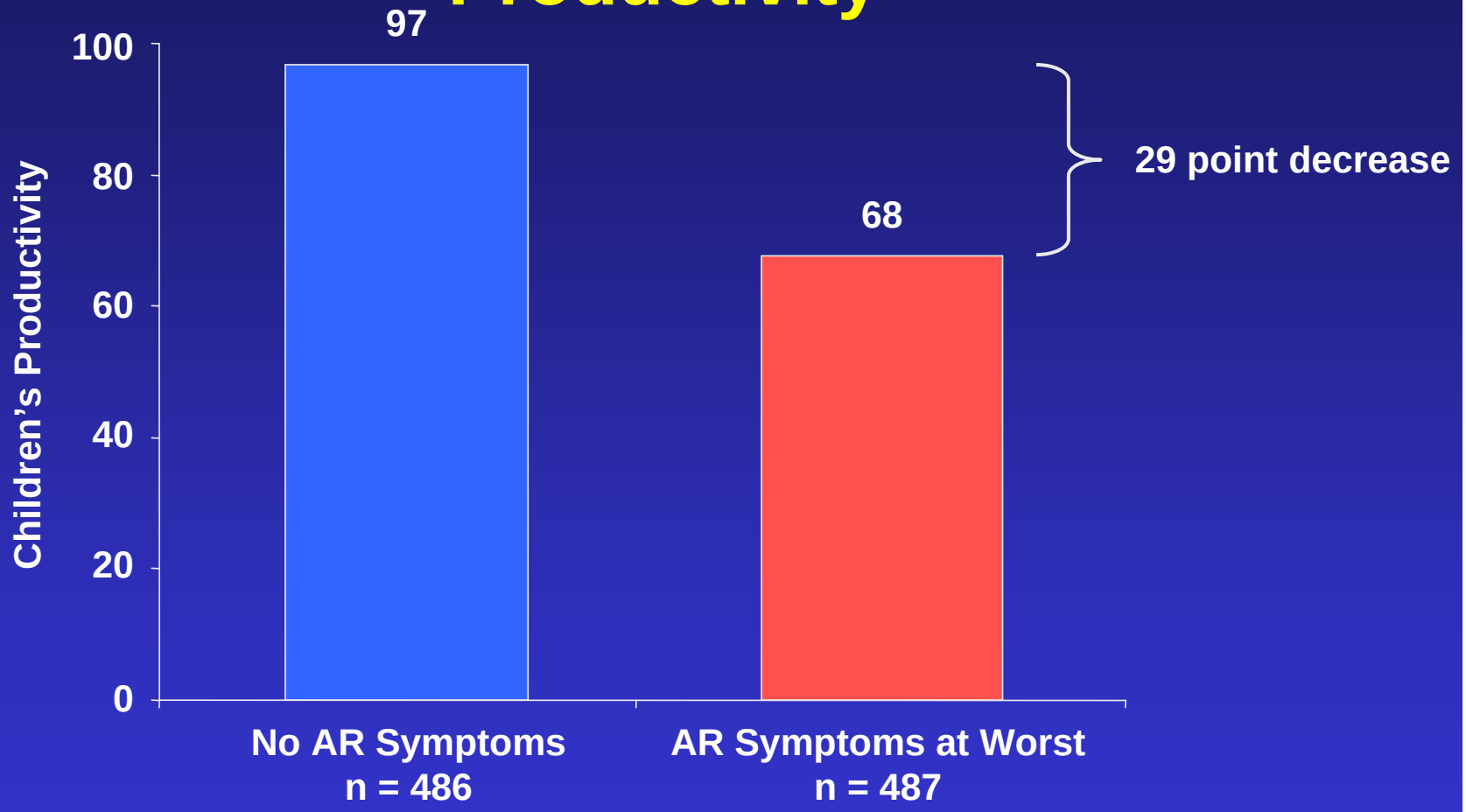
Parent Perceptions on the Effect of Nasal Allergy Symptoms on Children's Productivity



Thinking about your child's ability to do things (he/she) wants to do—on a scale of 0 to 100, where 100 means 100% able:
Where would you rank (his/her) ability on days when (he/she) doesn't have nasal allergy symptoms?
Where would you rank your child's ability on the same scale of 0 to 100 when (his/her) nasal allergies are at their worst?

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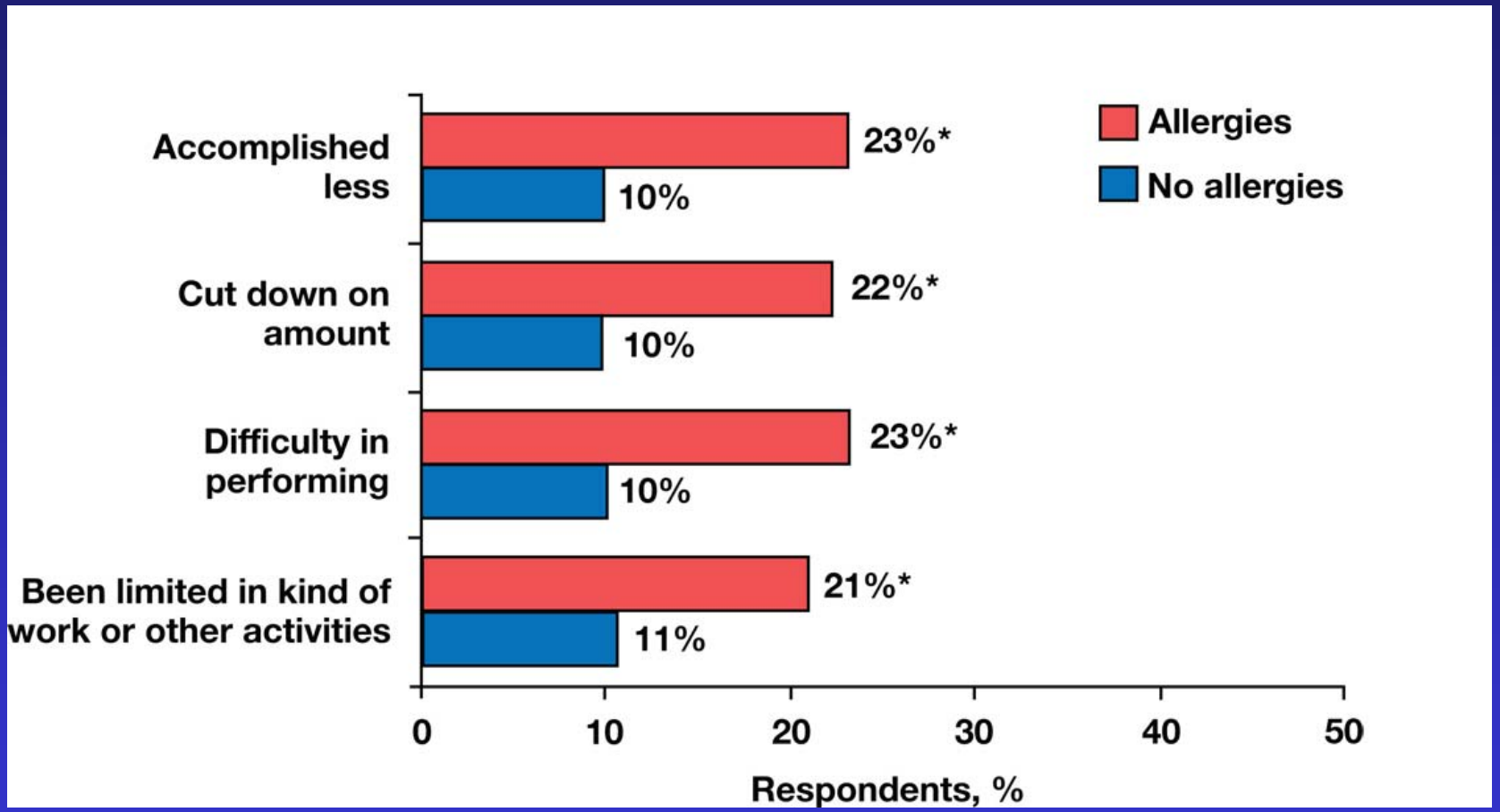
Parent Perceptions on the Effect of Nasal Allergy Symptoms on Type and Amount of Work Performed by Children



*P<0.05

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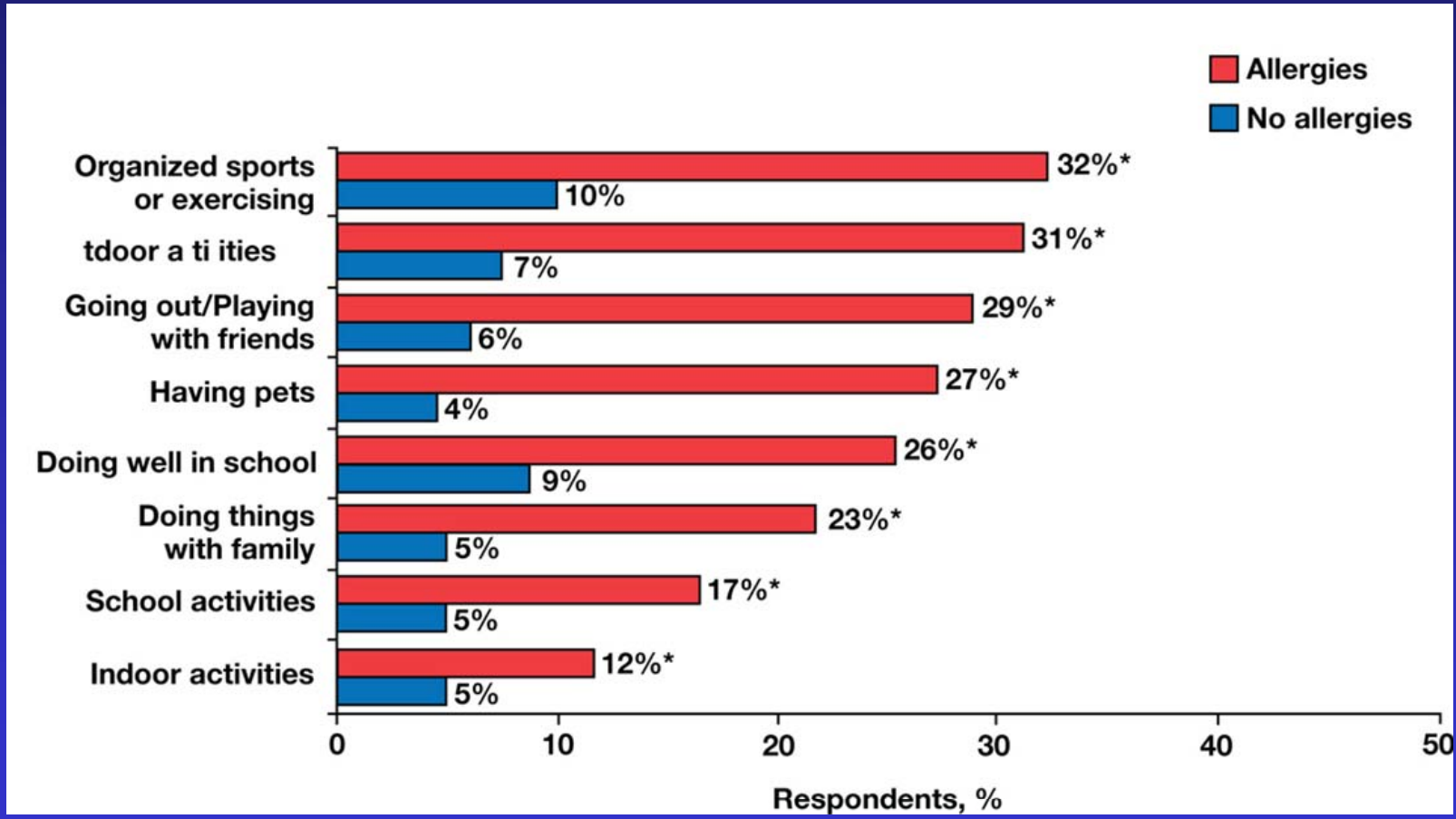
Parent Perceptions on the Effect of Nasal Allergy Symptoms on Children's Activities



*P<0.05

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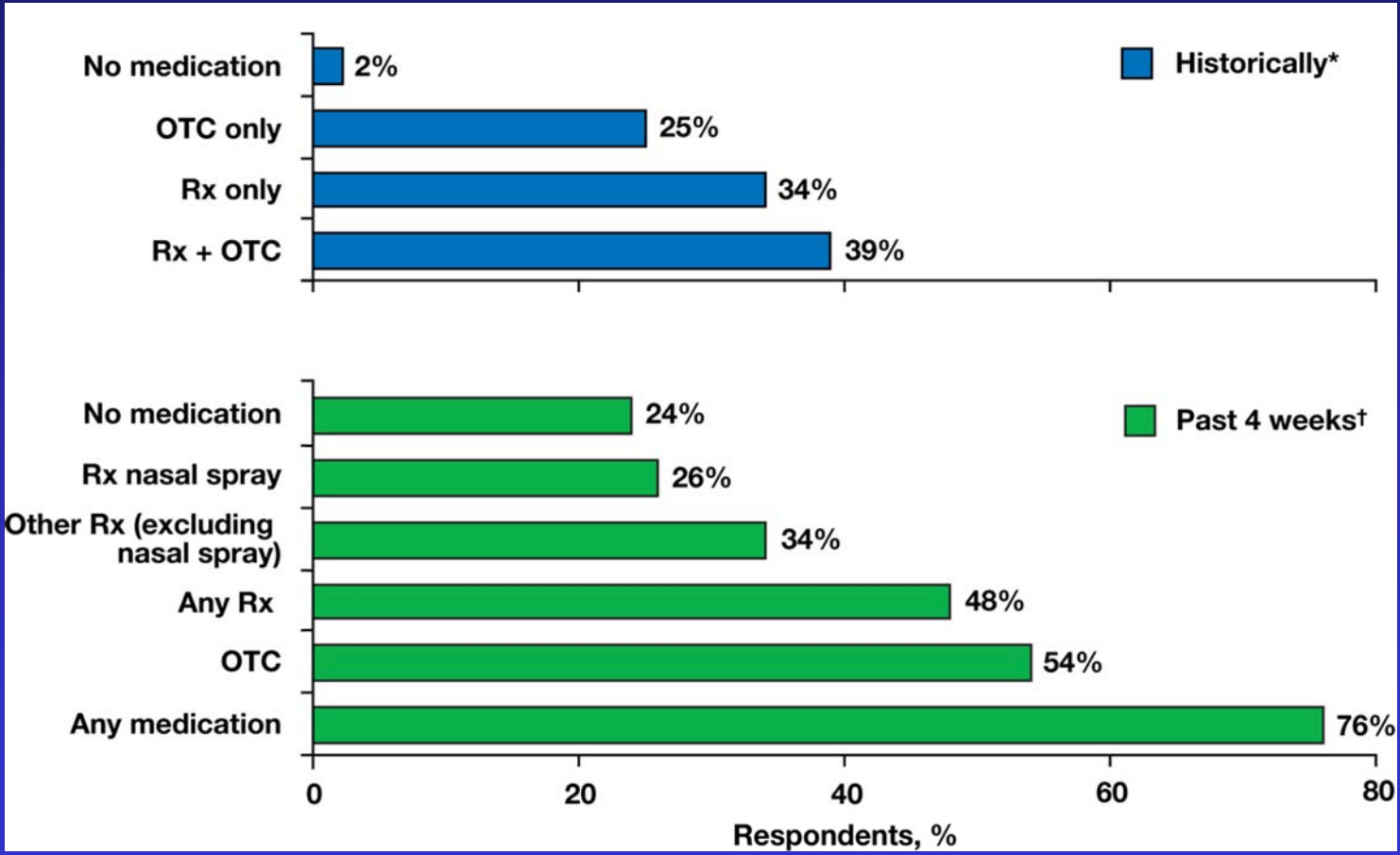
Percentage of Children Receiving Medications to Treat Nasal Allergy Symptoms



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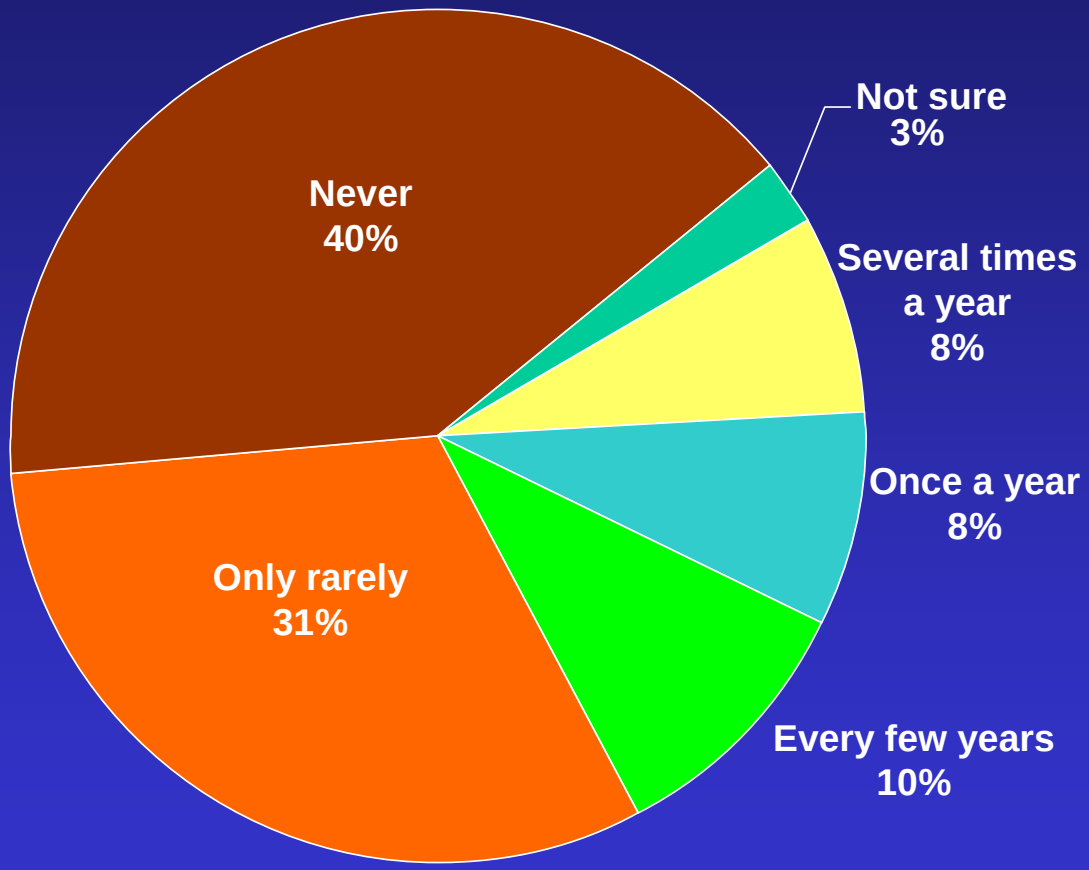
Change of Children's Prescription Medication



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Pharmacotherapy for Children

- Oral antihistamines
- Intranasal antihistamines
- Intranasal corticosteroids

Oral Antihistamines

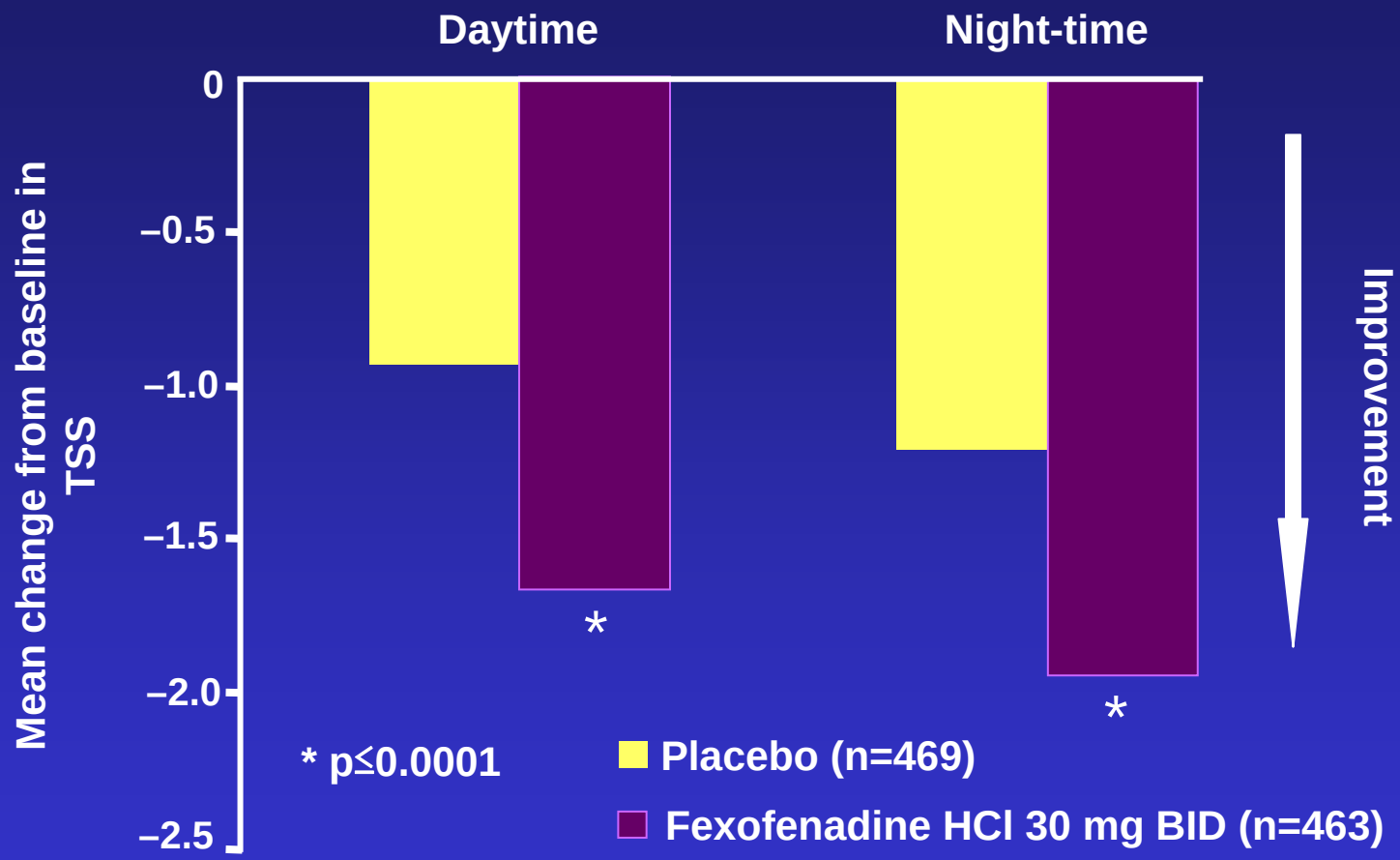
- 1st generation agents
- 2nd generation agents
  - Cetirizine
  - Levocetirizine
  - Loratadine
  - Ebastine
  - Desloratadine
  - Fexofenadine

Key efficacy fexofenadine SAR study

- **Aim:**
  - **Assess effect of fexofenadine HCl 30 mg BID compared with placebo across all SAR symptoms in children 6-11 years old**
- **Methods:**
  - **Placebo-controlled, parallel-group study conducted in 148 centers in 15 countries**
  - **935 children randomized to fexofenadine HCl 30 mg BID (n=464) or placebo (n=471) for 2 weeks**
  - **Primary efficacy variable**
    - Mean change from baseline in the average PM-reflective TSS throughout the double-blind treatment period**.**
- **Efficacy results:**
  - **Significant reductions in TSS and all individual symptom scores compared with placebo at all time points**

Wahn U et al. J Allergy Clin Immunol 2003;111:763–9.

Efficacy in children 6–11 years: TSS

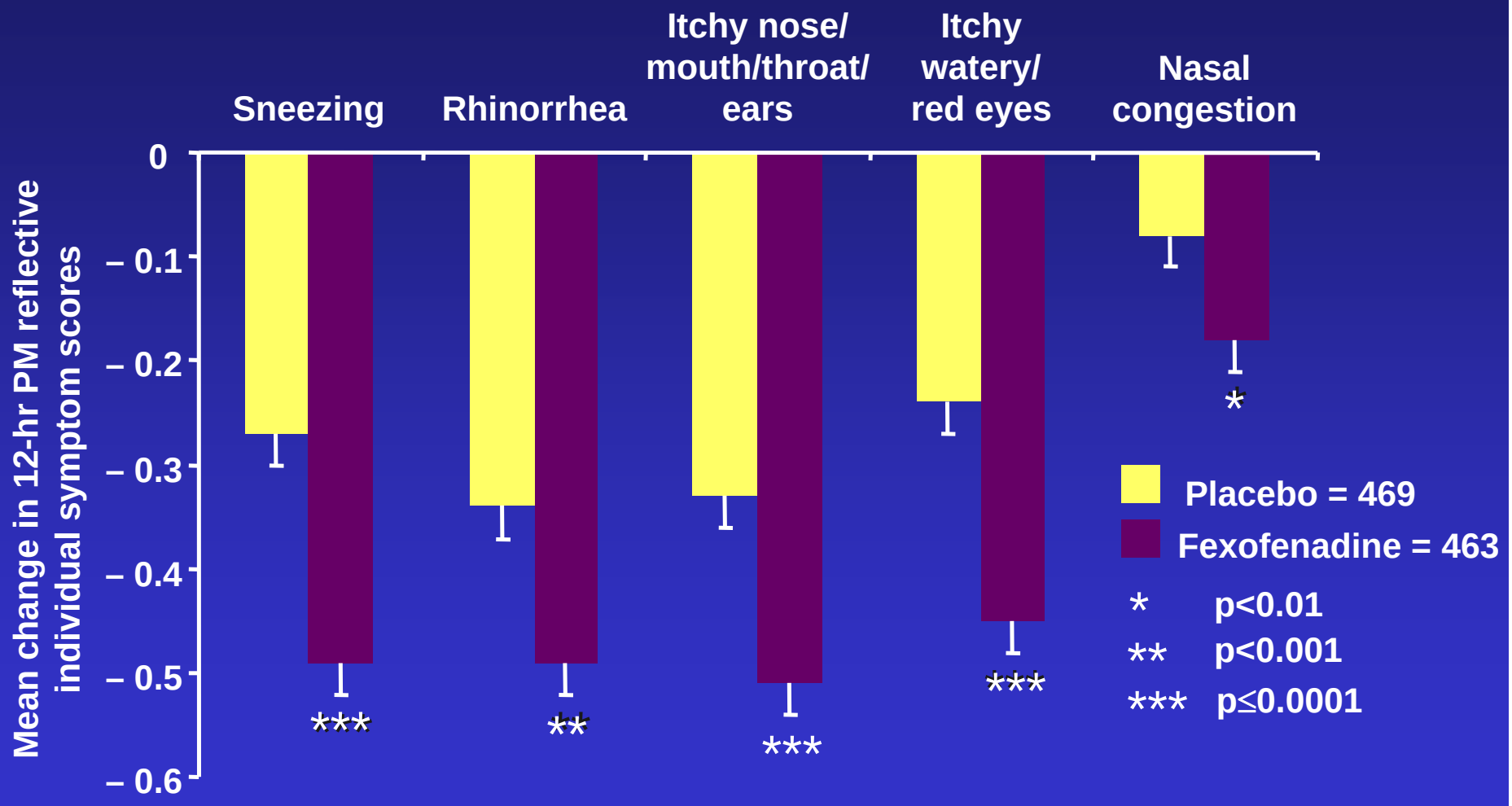


Baseline scores for fexofenadine and placebo, respectively, were: 7-pm reflective TSS 6.8, 7.1; 7-am reflective TSS 6.5, 6.7. Data are from the mITT population

TSS= Total Symptom Score

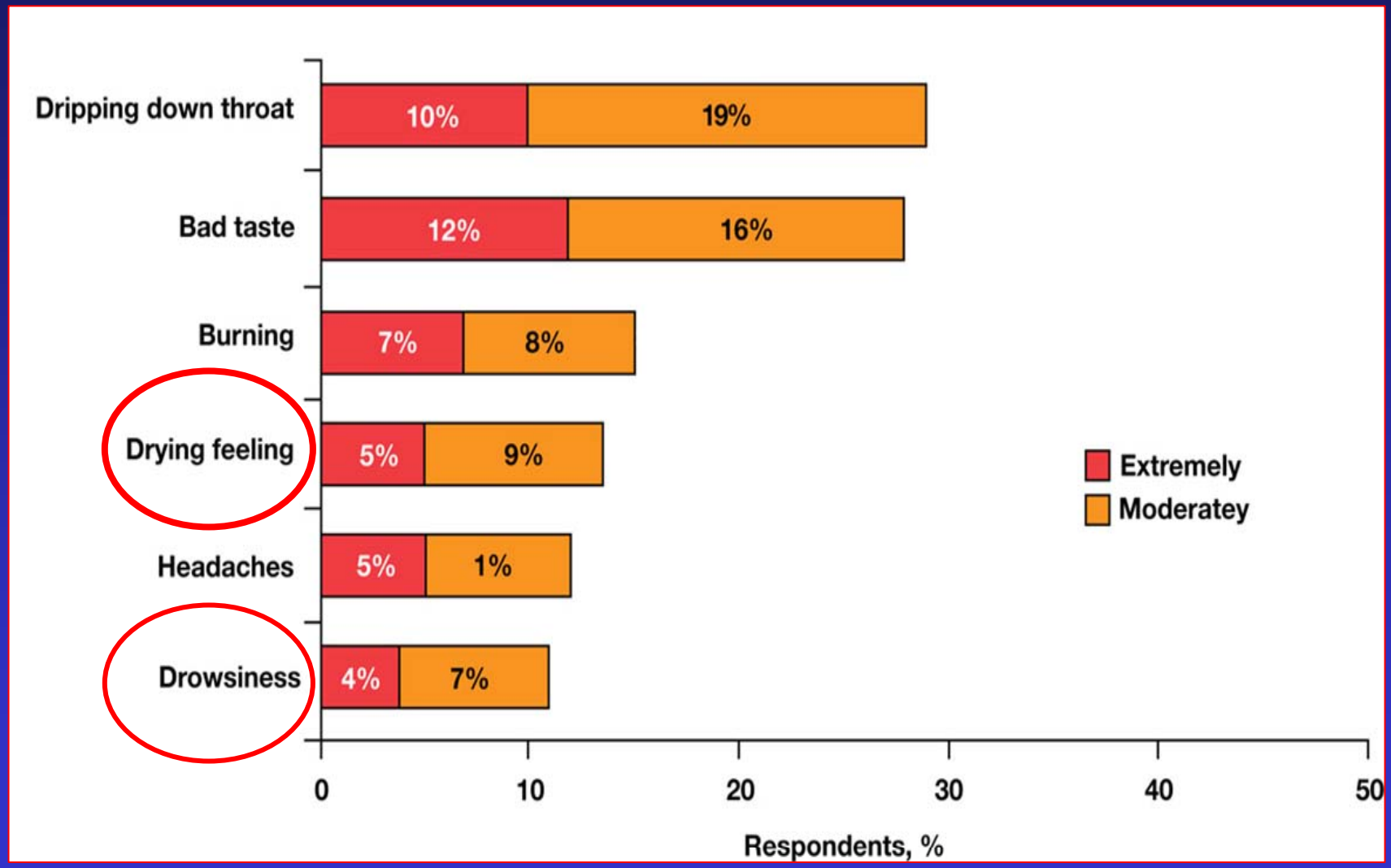
Wahn U et al. J Allergy Clin Immunol 2003;111:763–9.

Fexofenadine relieves all AR symptoms



Wahn U et al. J Allergy Clin Immunol 2003;111:763–9.

Most Bothersome Attributes of Nasal Allergy Medications in Children



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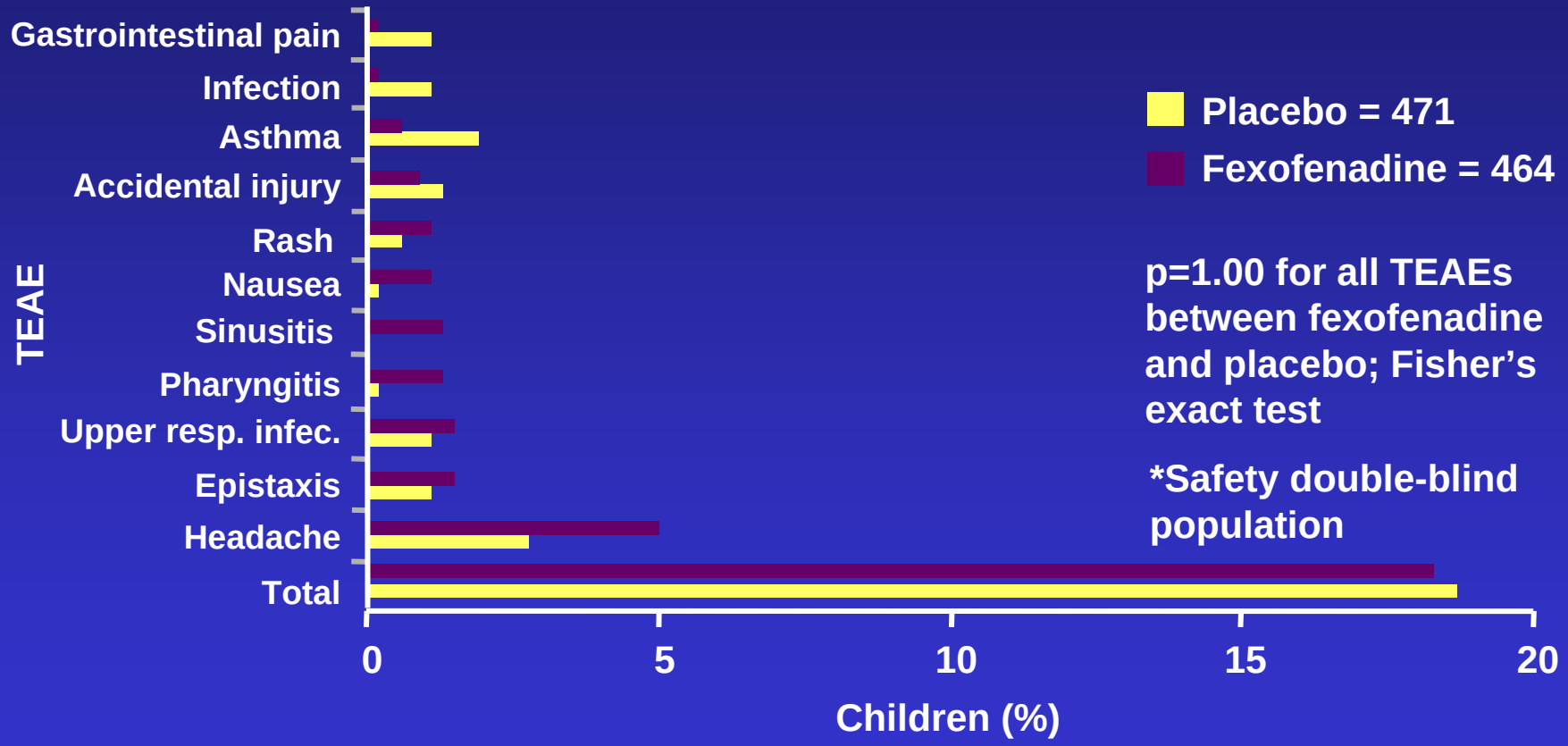
Adverse-event profile of fexofenadine
30 mg BID similar to placebo

Most frequent treatment-emergent adverse events (TEAEs) (>1%)*



The frequency of TEAE was similar beween the fexofenadine (18.3%) and the placebo (18.7)

Wahn U et al. J Allergy Clin Immunol 2003;111:763–9.

Safety of fexofenadine in children: pooled safety analysis

- Data pooled from three, double-blind studies examining fexofenadine HCl 30 mg and 60 mg BID in children 6–11 years (n>800)
  - Fexofenadine HCl 30mg BID, n = 673
  - All fexofenadine treated groups, n =1110
  - Placebo, n = 700
- Incidences of AEs, and discontinuations due to AEs, were low and similar across treatment groups
- 24.4% of subjects in the placebo group reported AEs compared with 24.1% for fexofenadine HCl 30 mg BID, and 28.4% for all fexofenadine-treated groups

Meltzer EO et al. Pediatr Allergy Immunol 2004;15:253–60.

Safety of fexofenadine in children 6-11 y: pooled safety analysis

- The most common AE overall was headache
  - 4.3%, (30/700), 5.8% (39/673) and 7.2% (80/1110) for placebo, fexofenadine HCl 30 mg BID and any fexofenadine dose, respectively

- Treatment-related AEs were similar across treatment groups
  - No sedation detected
  - No clinically relevant changes in vital signs data
  - No effect on QTc interval

Meltzer EO et al. Pediatr Allergy Immunol 2004;15:253–60.

Safety and tolerability of fexofenadine in younger children

- **Children aged 2–5 yrs (Milgrom 2007)**
  - Placebo-controlled, parallel-group study of fexofenadine HCl 30 mg BID (n=222), or placebo (n=231) x2 weeks
    - **No clinically meaningful differences between fexofenadine and placebo in pattern or intensity of TEAEs**
- **Children aged 6 mos–2 yrs (Hampel, 2007)**
  - Two placebo-controlled, parallel-group studies
    - Fexofenadine HCl 30 mg BID (n=108) or placebo (n=110)
    - Fexofenadine HCl 15 mg BID (n=85) or placebo (n=89)
  - **AE profile of fexofenadine similar to placebo**
    - Number of AE
      - **Fexofenadine: 40.0%; placebo: 42.7%**
      - **Fexofenadine: 35.2%; placebo: 52.7%**

Fexofenadine is indicated in SAR in children 2 to 11 years of age.
In urticaria from 6 months of age

Milgrom H et al, ,Ann Allergy Asthma Immunol. 2007;99:358–363
Hampel FC, et al. Ann Allergy Asthma Immunol. 2007;99:549–554.

Intranasal Antihistamines

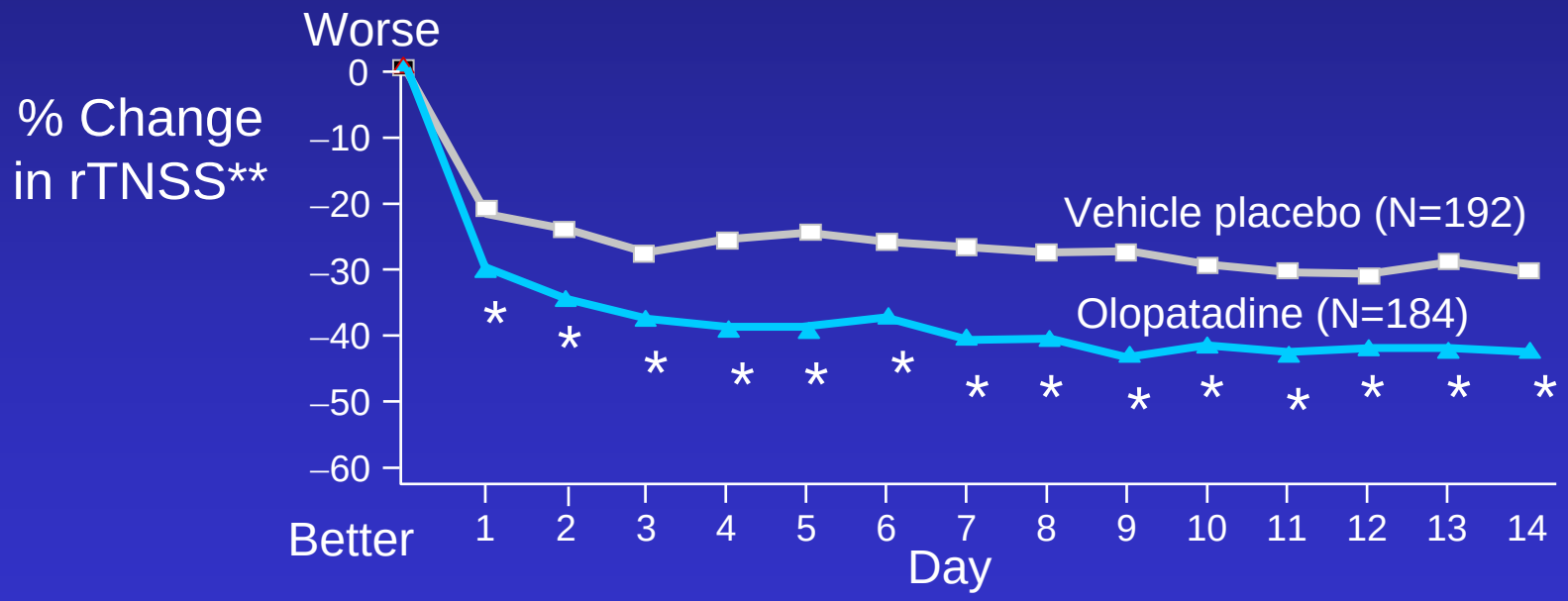
- Azelastine
  - No efficacy trials in children <12 years
  - Dose 1 spray/nostril BID 5-11 years*
  - Dose 1-2 sprays/nostril BID >12 years*
- Olopatadine
  - No efficacy trials in children <12 years
  - Dose 1 spray/nostril BID 6-11 years*
  - Dose 2 sprays/nostril BID >12 years*

*Approved by FDA

Olopatadine 0.6% Nasal Spray for SAR

Nasal Symptoms

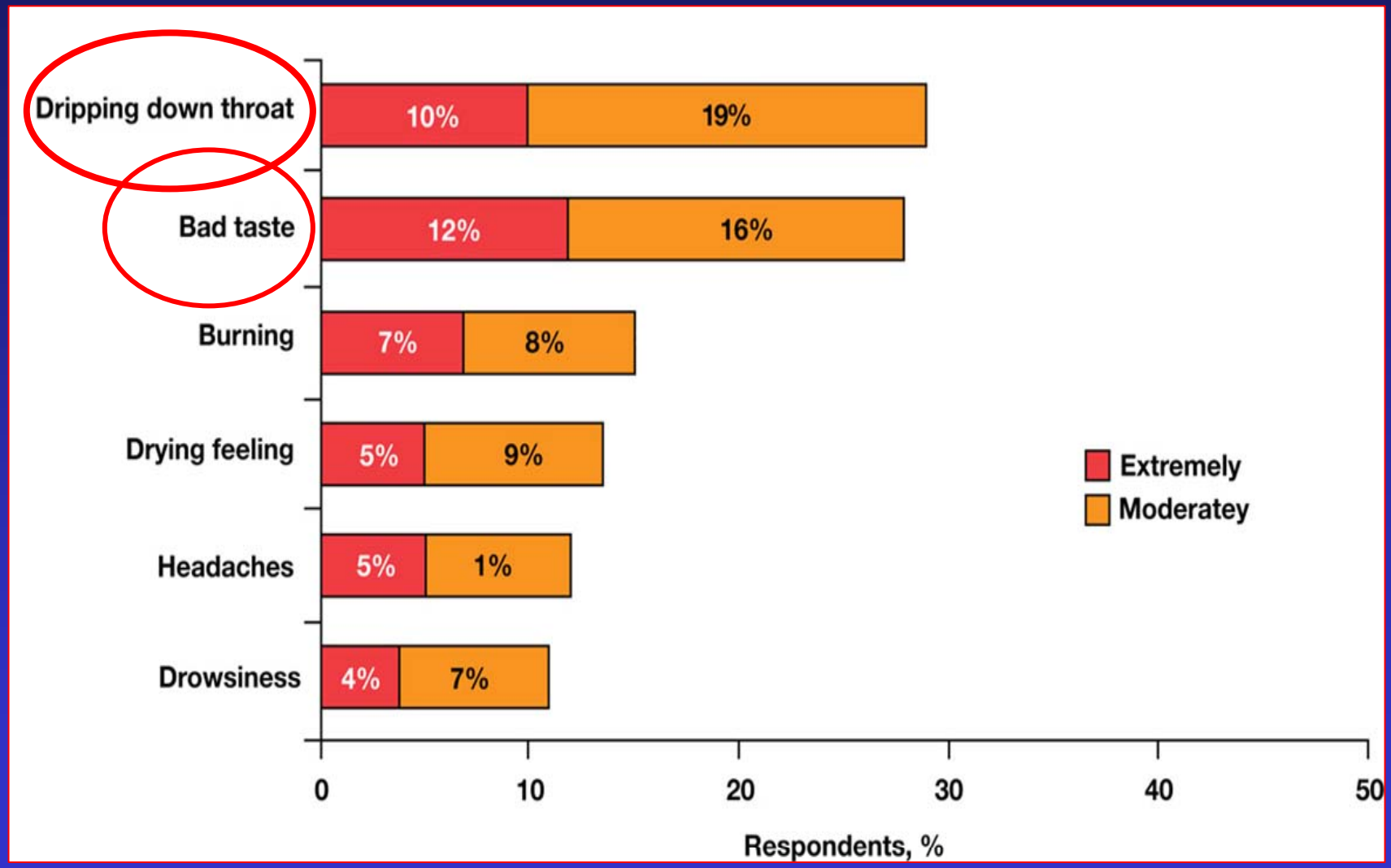
BID Tx for 14 Days in patients ≥ 12 yr with fall SAR



**p<0.05 olopatadine vs. placebo*
***rTNSS=Total Nasal Sx Score (0=absent to 3=severe)*

Meltzer et al. *Ann Allergy Asthma Immunol* 2005;95:600-6.

Most Bothersome Attributes of Nasal Allergy Medications in Children



Meltzer EO, et al. Burden of allergic rhinitis
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Olopatadine Nasal Spray Adverse Events in Pediatric Patients 6 to 11 Years of Age

Adverse Events >1%	Olopatadine Nasal Spray (N=298)	Vehicle Nasal Spray (N=297)
Epistaxis*	17 (5.7%)	11 (3.7%)
Headache	13 (4.4%)	11 (3.7%)
Upper respiratory tract infection	8 (2.6%)	0 (0.0%)
Bitter taste	3 (1.0%)	0 (0%)
Pyrexia	4 (1.3%)	3 (1.0%)
Rash	4 (1.3%)	0 (0.0%)

*Defined as a “fleck of blood” apparent on nasal examination.

PATANASE® Nasal Spray Package Insert

Intranasal Corticosteroids

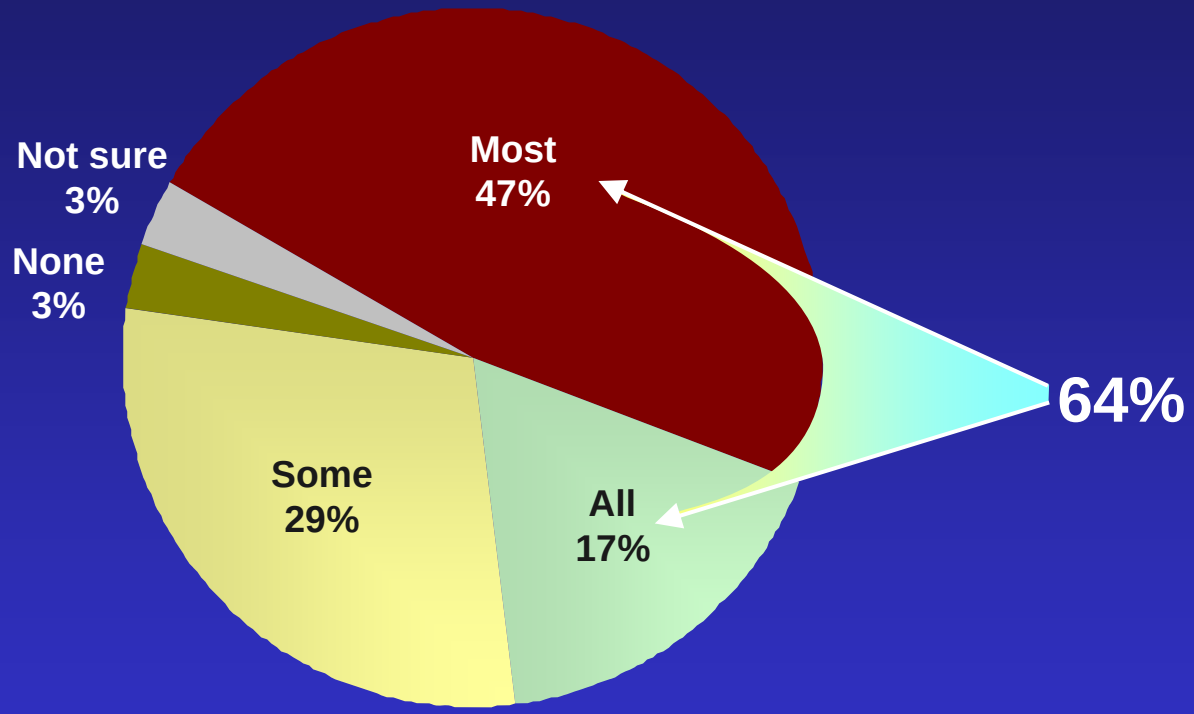
- **Aqueous intranasal corticosteroids**
  - Beclomethasone dipropionate
  - Budesonide
  - Ciclesonide
  - Flunisolide
  - Fluticasone furoate
  - Fluticasone propionate
  - Mometasone furoate
  - Triamcinolone acetonide

Aerosol intranasal corticosteroids (HFA)

  - Beclomethasone dipropionate
  - Ciclesonide

Drugs@FDA. US Food and Drug Administration. http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm. Accessed February 27, 2009.

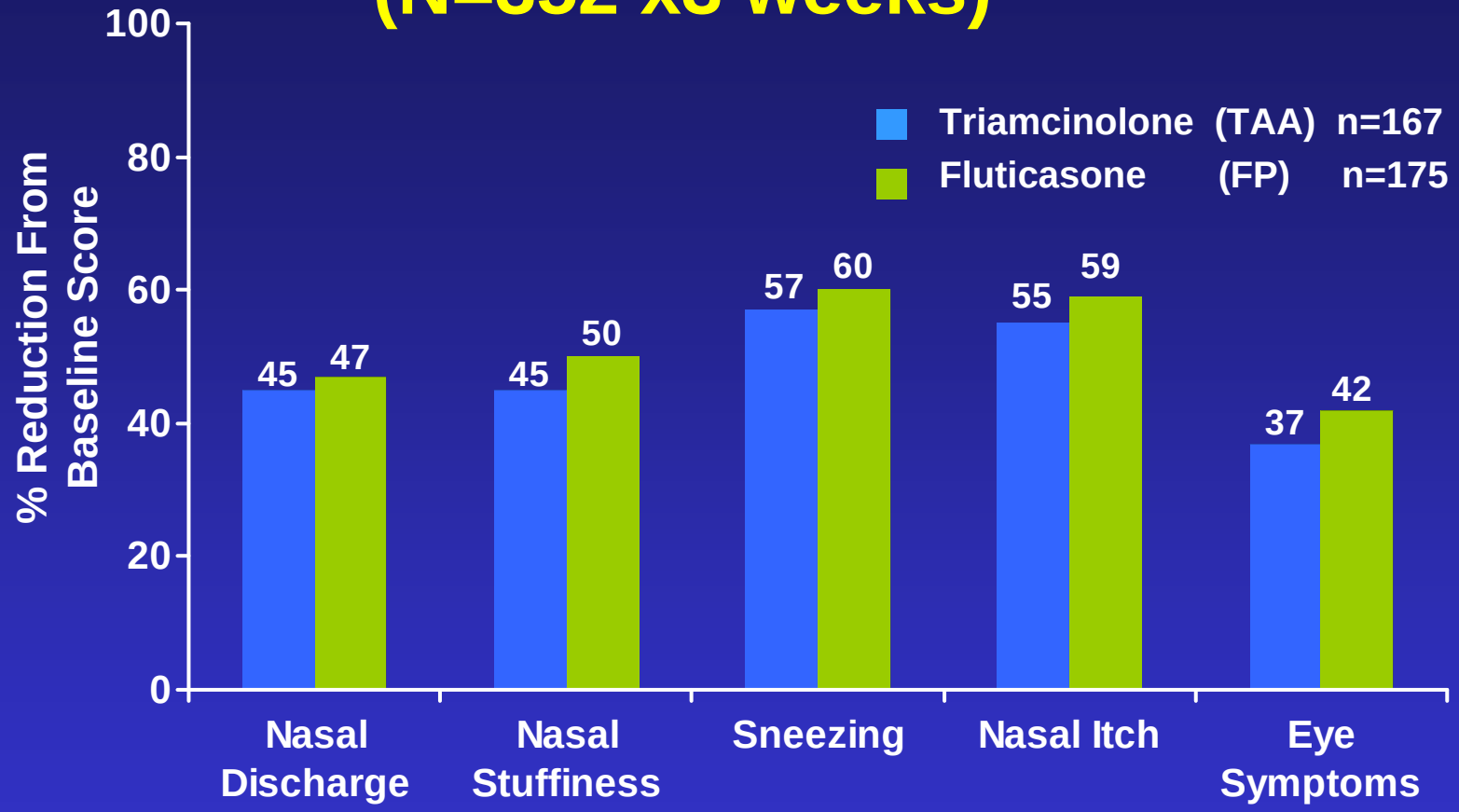
Intranasal Corticosteroids Provide Relief to Pediatric Nasal Allergy Sufferers



Does your child's current prescription nasal spray give relief from all symptoms, most symptoms, some symptoms, or no symptoms?
(Base: Uses Intranasal Corticosteroid, n=129)

Pediatric Allergies in America Survey Meltzer EO, et al. J Allergy Clin Immunol 2009
Available at: http://www.myallergiesinamerica.com/Alergies_website_v13.swf

Comparable Efficacy of Intranasal Steroids (TA-FP) in SAR in Adults (N=352 x3 weeks)



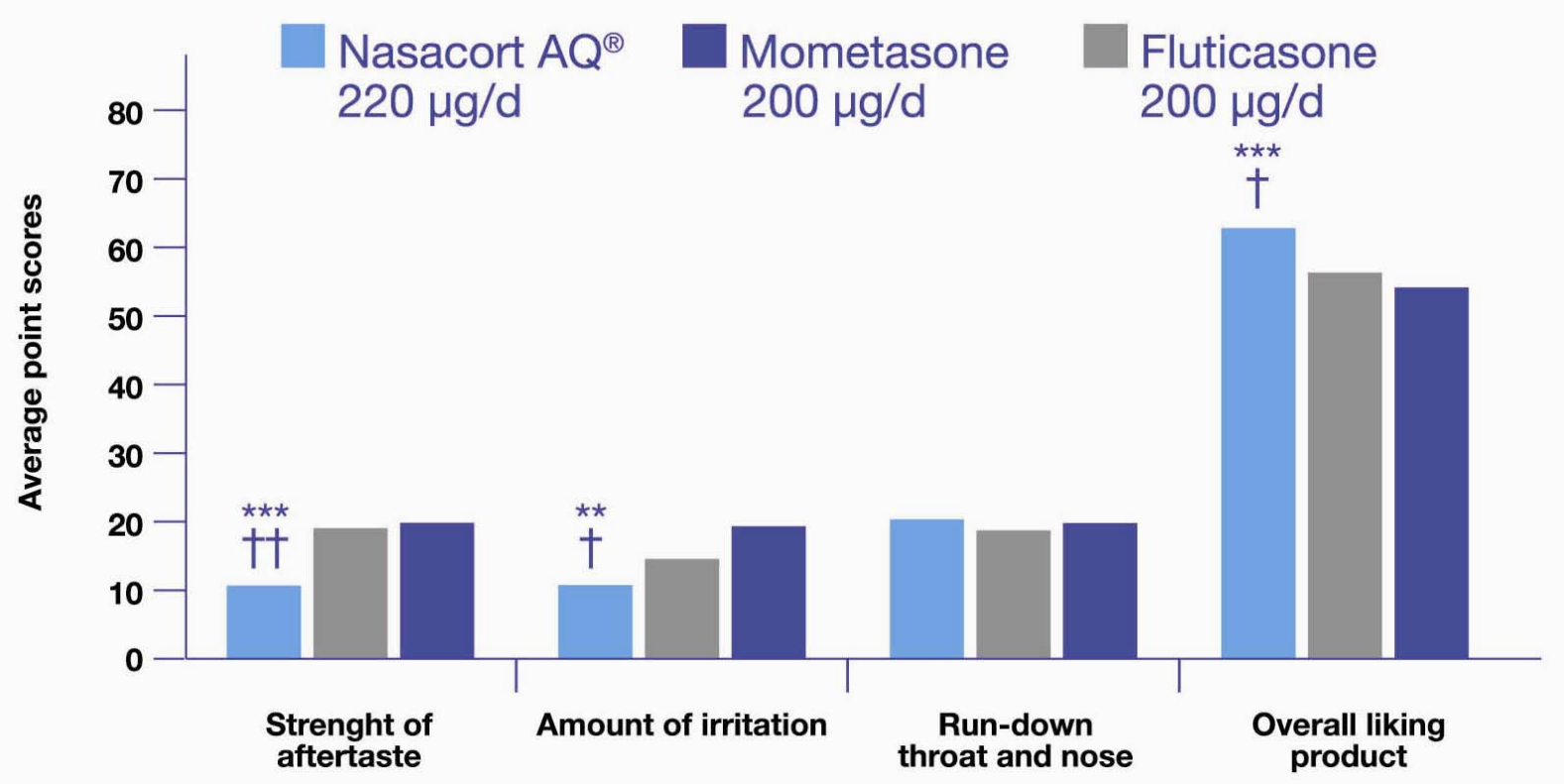
p = Not significant for any individual symptom

Adverse events occurred in 138 TAA patients (80.2%) and 152 FP patients (84.4%)

Primary efficacy variable: mean total nasal symptom score (sum individual nasal symptom scores)

Gross G et al. Ann Allergy Asthma Immunol. 2002;89:56-62.

Triamcinalone is significantly preferred by patients compared to other nasal corticosteroids



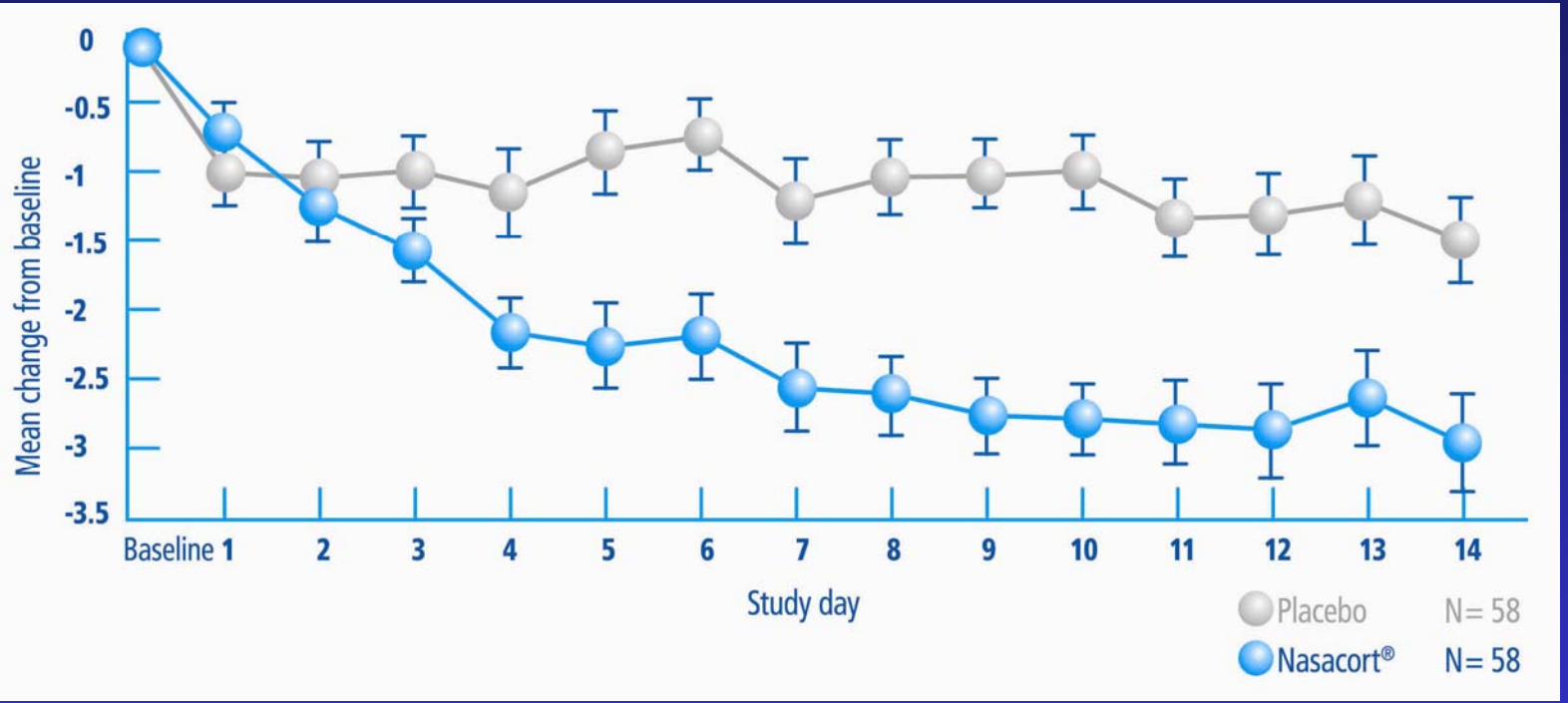
NASACORT® vs Mometasone Furoate ** p ≤0.01 *** p ≤ 0.001; NASACORT® vs Fluticasone Propionate † p ≤ 0.05 †† p ≤ 0.01

Mean nasal spray evaluation questionnaire scores two minutes after administration
(Adapted from Bachert C, 2002)

Multicenter, DB, controlled, cross-over study in 95 patients (ITT population) with Allergic Rhinitis (Perennial or Seasonal)

Bachert C et al, Ann Allergy Asthma Immunol 2002; 89:292-97

Triamcinalone Significantly Decreases SAR Nasal Index in Children ages 6-11 years



p < 0.05 versus placebo at week 1 & at week 2 (for one-tailed t test)

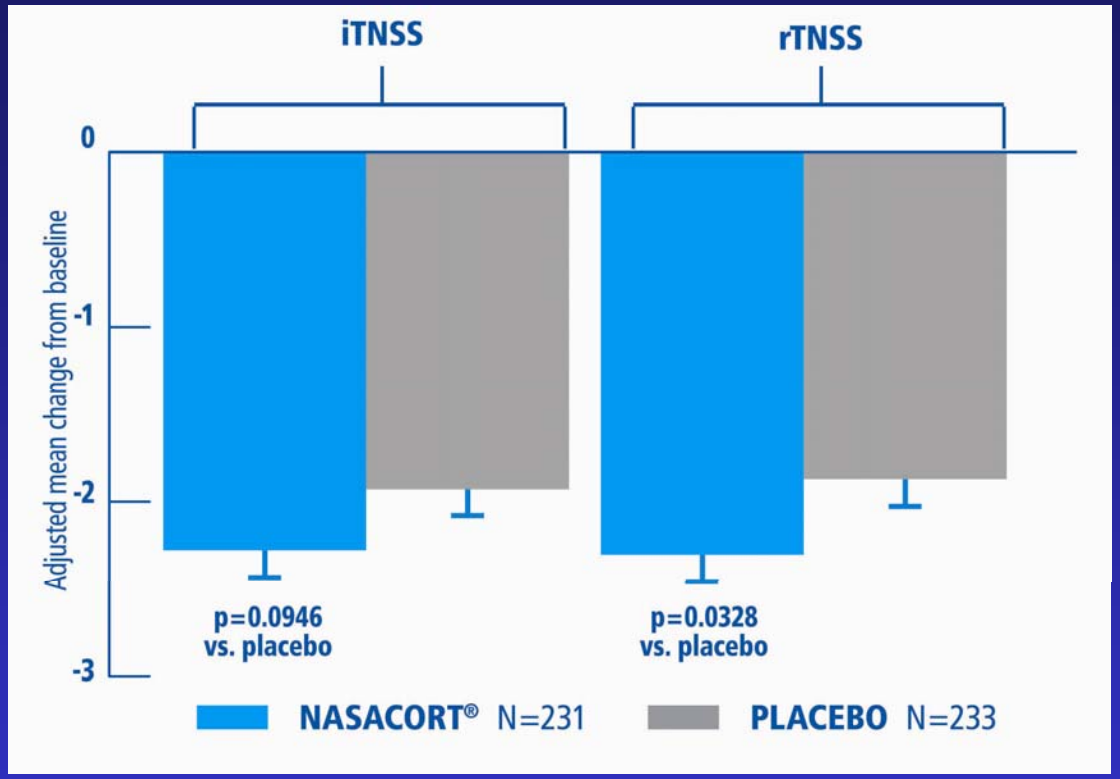
Daily mean changes (±SE) from baseline in nasal index over 2 week treatment period

No serious adverse events reported:
31 in triamcinolone, 22 in the placebo reported AEs
Most were mild

Multicenter, DB, PBO controlled, 2 –weeks study in children 6-11 yrs
Primary endpoint: Nasal index: sum of symptom scores: nasal stuffiness, nasal discharge, sneezing.

Banov H et al, Clin Ther 1996;18: 265-272

Triamcinolone Significantly Decreases PAR Symptoms in Children ages 2-5 years

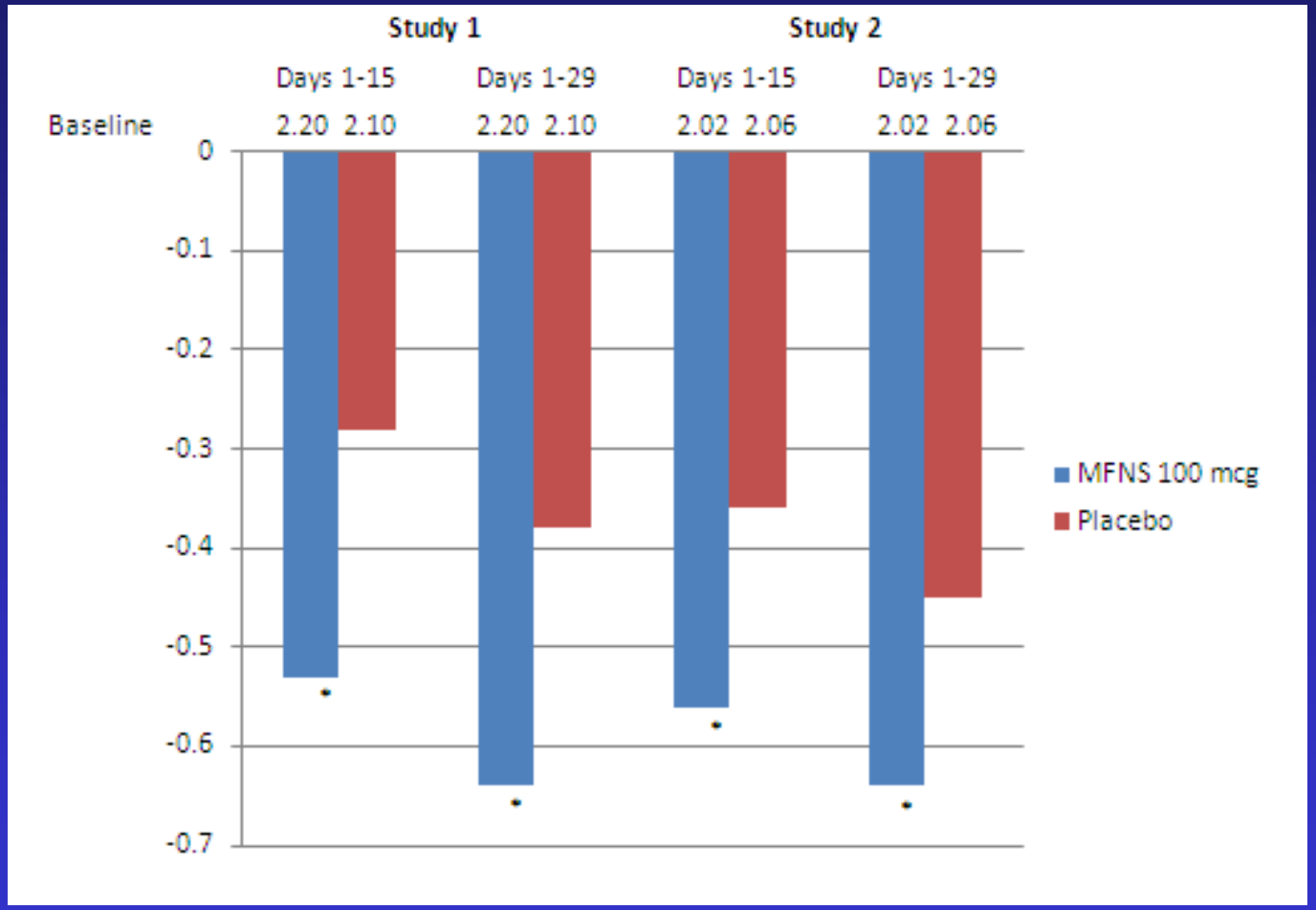


Possibly related to study medication in the DB period: similar between the groups: triamcinolone:13 [5.5%]; placebo:20 [8.4%]

Multicenter, DB, 4- weeks (open phase 6 months), PC study in children ages 2-5 years with PAR 4-point scale: (0=symptom absent to 3=severe)
Primary endpoint: Change from baseline in the mean daily instantaneous total nasal symptom score (TNSS) over the double-blind treatment period

Weinstein S, Ann Allergy, Asthma Immunol, 2009: 102, 339-347

Children with SAR (Ages 6-11y) and PAR (Ages 3-11y): Changes from Baseline Congestion Score Days 1-15; 1-29



P<0.05 MFNS (mometasone furoate aqueous nasal spray) vs Pbo
Study 1 = SAR; Study 2 = PAR
Congestion = Primary end point

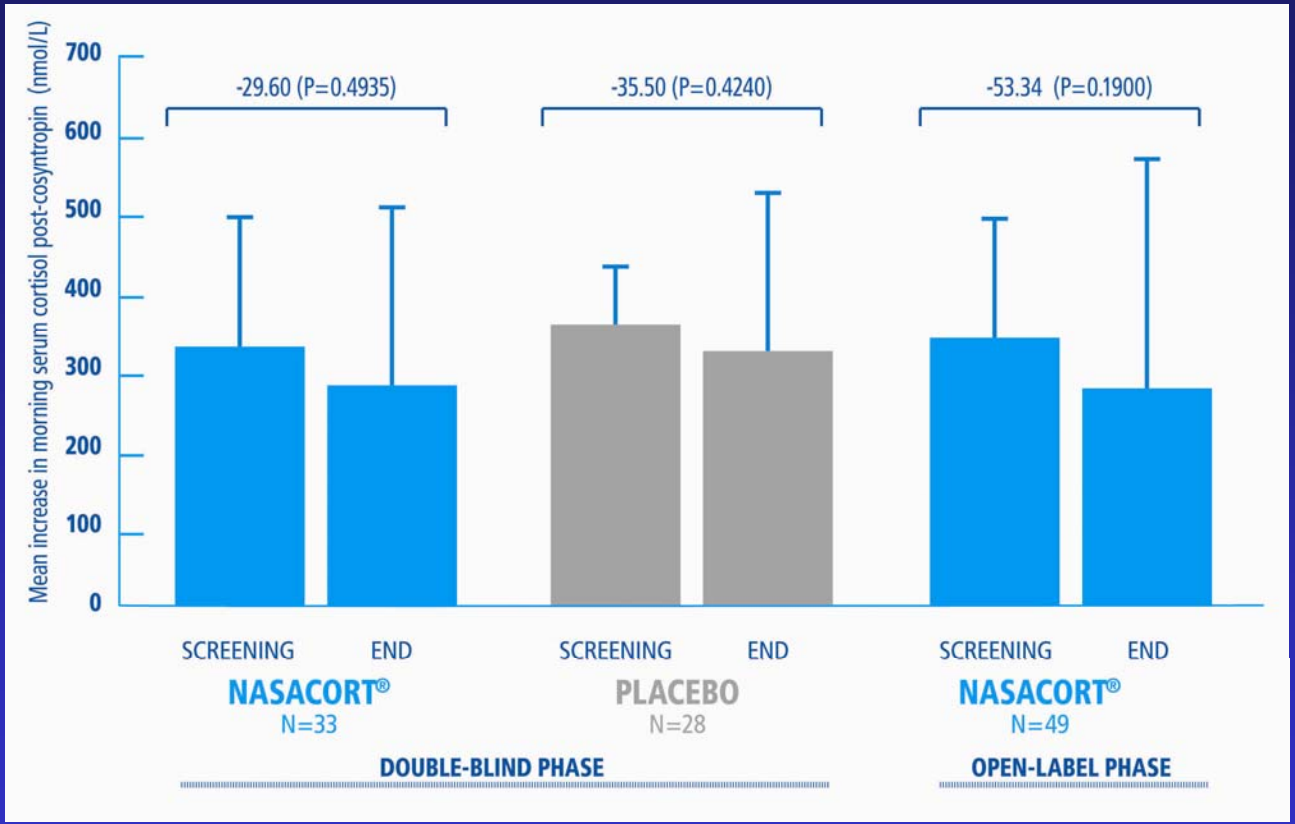
Baena-Cagnani C, et al. EAACI-PAAM 2011. In Abstract Book PAAM2011. Accessed Nov 2011.

Children with SAR (Ages 6-11y) and PAR (Ages 3-11y): Adverse Events

	Study 1 (SAR)		Study 2 (PAR)	
	MFNS 100 mcg (n=135)	**Placebo (n=136)**	**MFNS 100 mcg (n=190)**	**Placebo (n=191)**
AEs reported by ≥5% of patients, n (%)	Fever, 9 (7%) Headache, 30 (22%) Asthma, 8 (6%) Coughing, 7 (5%) Epistaxis, 12 (9%) Pharyngitis, 9 (7%) Vomiting, 7 (5%)	Fever, 11 (8%) Headache, 26 (19%) Asthma, 12 (9%) Coughing, 11 (8%) Epistaxis, 10 (7%) Sneezing, 7 (5%)	Coughing, 27 (14%) Headache, 24 (13%) Fever, 16 (8%) Pharyngitis, 14 (7%) Epistaxis, 12 (6%)	Coughing, 33 (17%) Headache, 25 (13%) Fever, 15 (8%) Pharyngitis, 14 (7%) Epistaxis, 17 (9%) Viral infection, 14 (7%)

Baena-Cagnani C, et al. EAACI-PAAM 2011. In Abstract Book PAAM2011. Accessed Nov 2011.

Triamcinolone *vs* Placebo: Serum cortisol levels are not altered

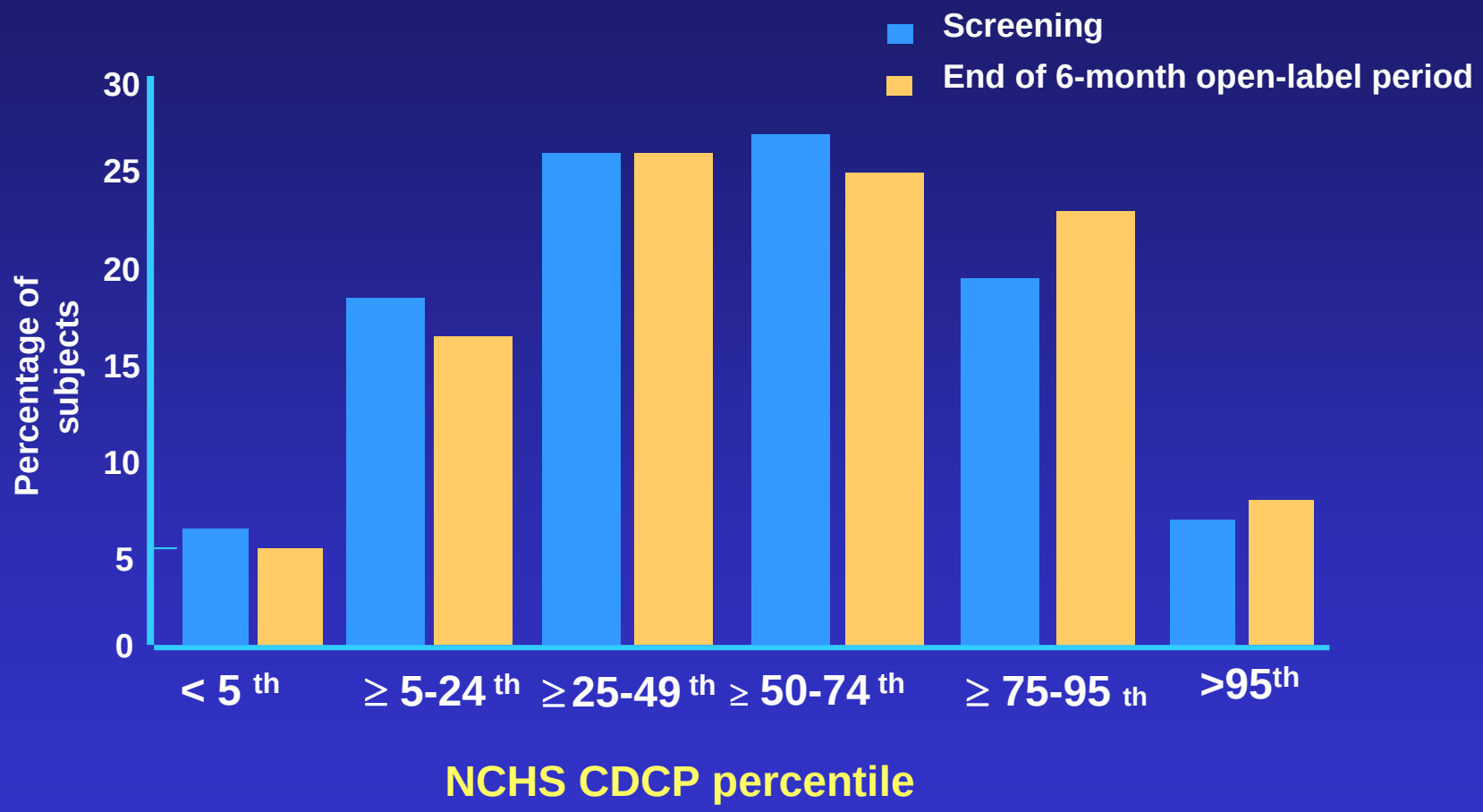


Mean increase in morning serum cortisol level after cosyntropin infusion in the cosyntropin-evaluable population. Error bars represent SD.

Multicenter, randomized, double-blind, placebo-controlled, parallel-group study immediately followed by an open-label extension period

Weinstein S, Ann Allergy, Asthma Immunol, 2009: 102, 339-347

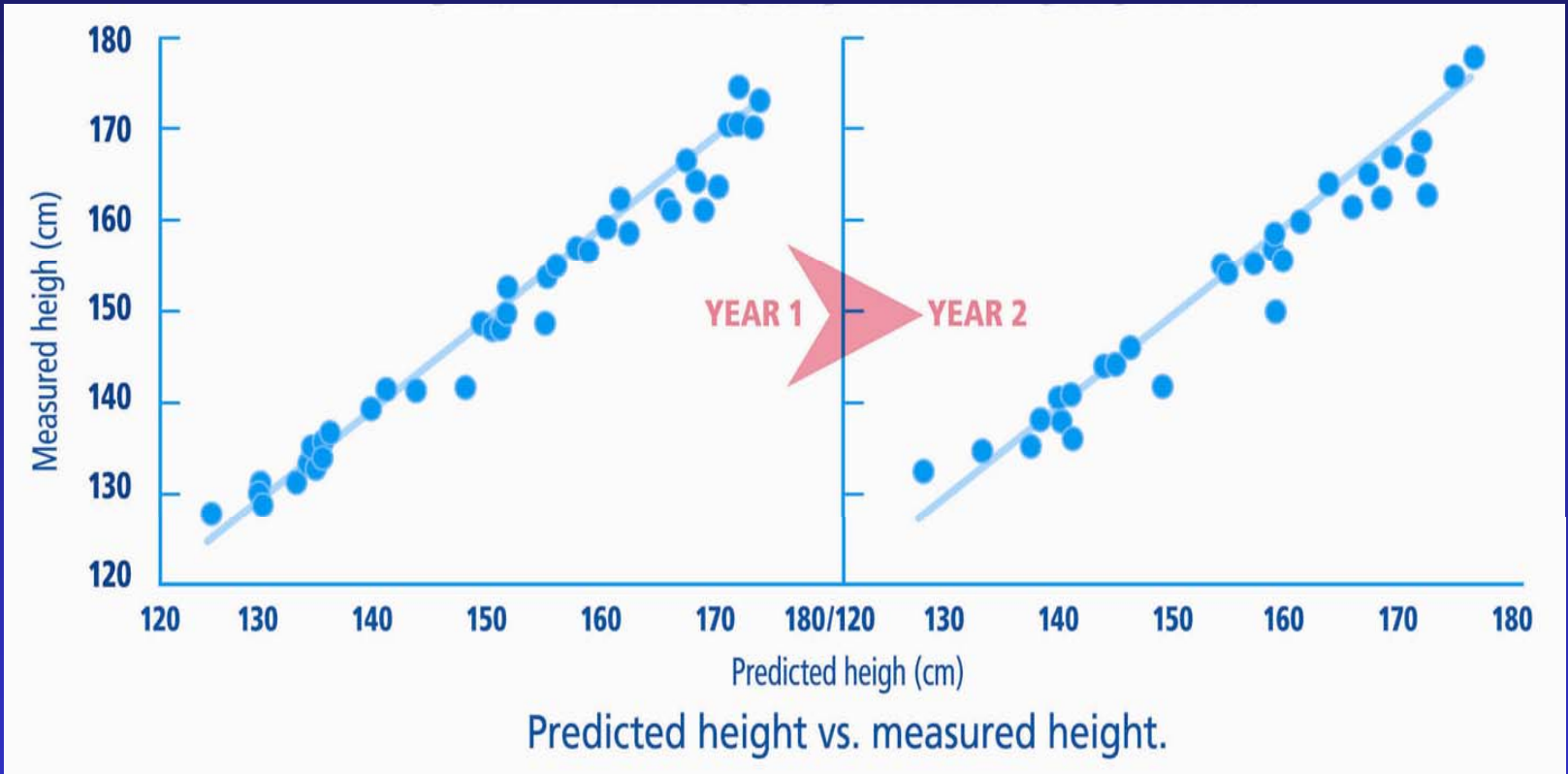
Triamcinalone *vs* Placebo: Stature Remains Stable Throughout 6 months Treatment Period



Distribution of 353 patients by stature-for-age percentile at baseline and at the end of the 6-month open-label period based on the National Center for Health Statistics, Centers for Disease Control and Prevention (NCHS CDCP) standards

Weinstein S, Ann Allergy, Asthma Immunol, 2009: 102, 339-347

Intranasal Triamcinalone Does Not Adversely Affect Children Long Term Growth



Predicted height vs. measured height.

Monocenter, open-label, non-randomized, prospective study of the long term effect of triamcinolone on statural growth in 39 children from 6-14 years in a 2 year-study

Skoner DP, Ann Allergy Asthma Immunol, 2008, 101 (4):431-36

Thank you!