Natural History of Asthma

이세원

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Content

1. Wheezing during 1st 6 years
2. Wheezing in later childhood
3. Adult onset Asthma

“Will this child with persistent asthma outgrow his/her disease?”

“If so, what can be done to help this?”

The New England
Journal of Medicine

Volume 332 JANUARY 19, 1995 Number 3

ASTHMA AND WHEEZING IN THE FIRST SIX YEARS OF LIFE

FERNANDO D. MARTINEZ, M.D., ANNE L. WRIGHT, PH.D., LYNN M. TAUSSIG, M.D., CATHARINE J. HOLBERG, M.SC., MARILYN HALONEN, PH.D., WAYNE J. MORGAN, M.D., AND THE GROUP HEALTH MEDICAL ASSOCIATES*

Enrolled (n = 1246)

With follow-up for lower respiratory tract illnesses in the first 3 years (n = 888)

With questionnaires on wheezing at 6 years of age (n = 1024)

With Both (n = 826)

Assessments in Infancy

Cord-serum IgE (n = 750)
Pulmonary-function testing at <6 months of age (n = 125)
Serum IgE at 9 months of age (n = 672)
Questionnaire at 1 year of age (n = 800)

Assessments at 6 Years of Age

Serum IgE (n = 460)
Pulmonary-function testing (n = 526)
Skin allergy testing (n = 629)

N Engl J Med 1995;332:133-8

Outcome of Asthma and Wheezing in the First 6 Years of Life

Follow-up through Adolescence

Wayne J. Morgan*, Debra A. Stern*, Duane L. Sherrill, Stefano Guerra, Catharine J. Holberg, Theresa W. Guilbert, Lynn M. Taussig, Anne L. Wright, and Fernando D. Martinez

Arizona Respiratory Center and Department of Pediatrics, University of Arizona Health Sciences Center, Tucson, Arizona; and National Jewish Medical and Research Center and University of Colorado Health Sciences Center, Denver, Colorado

Healthy infants were enrolled at birth
Tucson Children's Respiratory Study in Tucson, Arizona (n=1,246)

≥1 physician-diagnosed wheezing lower respiratory illness (LRI) in the first 3 years of life

≥1 one episode of "parent reported wheeze during the past year for the child at age 6"

Am J Respir Crit Care Med Vol 172. pp 1253–1258, 2005

Wheeze Phenotype

Enrolled Children (n=1246)

↓

Children with complete information for wheezing lower respiratory illnesses through age 3 and wheeze at

	n	LRI by Age 3	Wheeze at Age 6
Never Wheeze	425	No	No
Transient Early Wheeze	164	Yes	No
Late Onset Wheeze	124	No	Yes
Persistent Wheeze	113	Yes	Yes

↙ ↓ ↘

Age 6
$V'_{max}FRC$ (n=526)

Age 11
FEF_{25-75}, FEV_1, FVC (n=542)
Questionnaire (n=762)
Skin Prick tests (n=609)

Age 16
FEF_{25-75}, FEV_1, FVC (n=426)
Questionnaire (n=606)
Skin Prick Tests (n=461)

Am J Respir Crit Care Med Vol 172. pp 1253–1258, 2005

Risk Factor of Transient Early Wheezing

Risk Factor	No	Transient Early Wheezing (N = 147)	Late-Onset Wheezing (N = 112)	Persistent Wheezing (N = 100)
Eczema				
Odds ratio (95% CI)	1.0	1.3 (0.7–2.5)	0.7 (0.3–1.6)	2.4 (1.3–4.6)
Prevalence (%)	7.7	10.2	6.3	18.0
Rhinitis apart from colds				
Odds ratio (95% CI)	1.0	1.1 (0.7–1.7)	1.7 (1.1–2.7)	2.0 (1.2–3.2)
Prevalence (%)	24.8	27.2	35.7	42.0
Maternal asthma				
Odds ratio (95% CI)	1.0	1.6 (0.8–3.2)	2.8 (1.4–5.5)	4.1 (2.1–7.9)
Prevalence (%)	6.7	10.2	16.1	22.0
Hispanic ethnic background				
Odds ratio (95% CI)	1.0	1.5 (0.9–2.7)	1.7 (0.9–3.1)	3.0 (1.6–5.5)
Prevalence (%)	10.7	13.6	14.3	22.0
Male sex				
Odds ratio (95% CI)	1.0	1.0 (0.7–1.5)	2.1 (1.3–3.4)	1.9 (1.2–3.0)
Prevalence (%)	42.7	44.2	61.6	61.0
Maternal smoking				
Odds ratio (95% CI)	1.0	2.2 (1.3–3.7)	1.6 (0.9–2.9)	2.3 (1.2–4.4)
Prevalence (%)	11.4	21.2	17.0	21.0

N Engl J Med 1995;332:133-8

Risk Factor of Late Onset Wheezing

Risk Factor	No Wheezing (N = 403)	Transient Ear Wheezing (N = 147)	Late-Onset Wheezing (N = 112)	Persistent Wheezing (N = 100)
Eczema				
Odds ratio (95% CI)	1.0	1.3 (0.7–2.5)	0.7 (0.3–1.6)	2.4 (1.3–4.6)
Prevalence (%)	7.7	10.2	6.3	18.0
Odds ratio (95% CI)	1.0	1.1 (0.7–1.7)	1.7 (1.1–2.7)	2.0 (1.2–3.2)
Prevalence (%)	24.8	27.2	35.7	42.0
Odds ratio (95% CI)	1.0	1.6 (0.8–3.2)	2.8 (1.4–5.5)	4.1 (2.1–7.9)
Prevalence (%)	6.7	10.2	16.1	22.0
Hispanic ethnic background				
Odds ratio (95% CI)	1.0	1.5 (0.9–2.7)	1.7 (0.9–3.1)	3.0 (1.6–5.5)
Prevalence (%)	10.7	13.6	14.3	22.0
Male sex				
Odds ratio (95% CI)	1.0	1.0 (0.7–1.5)	2.1 (1.3–3.4)	1.9 (1.2–3.0)
Prevalence (%)	42.7	44.2	61.6	61.0
Maternal smoking				
Odds ratio (95% CI)	1.0	2.2 (1.3–3.7)	1.6 (0.9–2.9)	2.3 (1.2–4.4)
Prevalence (%)	11.4	21.2	17.0	21.0

Rhinitis apart from colds

Maternal asthma

Male sex

N Engl J Med 1995;332:133-8

Risk Factor of Persistent Wheezing

Risk Factor	No Wheezing (N = 403)	Transient Early Wheezing (N = 147)	Late-On Wheezi (N = 11	Persistent Wheezing (N = 100)
Eczema				
Odds ratio (95% CI)	1.0	1.3 (0.7–2.5)	0.7 (0.3–1.6)	2.4 (1.3–4.6)
Prevalence (%)	7.7	10.2	6.3	18.0
Rhinitis apart from colds				
Odds ratio (95% CI)	1.0	1.1 (0.7–1.7)	1.7 (1.1–2.7)	2.0 (1.2–3.2)
Prevalence (%)	24.8	27.2	35.7	42.0
Maternal asthma				
Odds ratio (95% CI)	1.0	1.6 (0.8–3.2)	2.8 (1.4–5.5)	4.1 (2.1–7.9)
Prevalence (%)	6.7	10.2	16.1	22.0
Hispanic ethnic background				
Odds ratio (95% CI)	1.0	1.5 (0.9–2.7)	1.7 (0.9–3.1)	3.0 (1.6–5.5)
Prevalence (%)	10.7	13.6	14.3	22.0
Male sex				
Odds ratio (95% CI)	1.0	1.0 (0.7–1.5)	2.1 (1.3–3.4)	1.9 (1.2–3.0)
Prevalence (%)	42.7	44.2	61.6	61.0
Maternal smoking				
Odds ratio (95% CI)	1.0	2.2 (1.3–3.7)	1.6 (0.9–2.9)	2.3 (1.2–4.4)
Prevalence (%)	11.4	21.2	17.0	21.0

N Engl J Med 1995;332:133-8

Maximal Exp. Flow at 6 years old

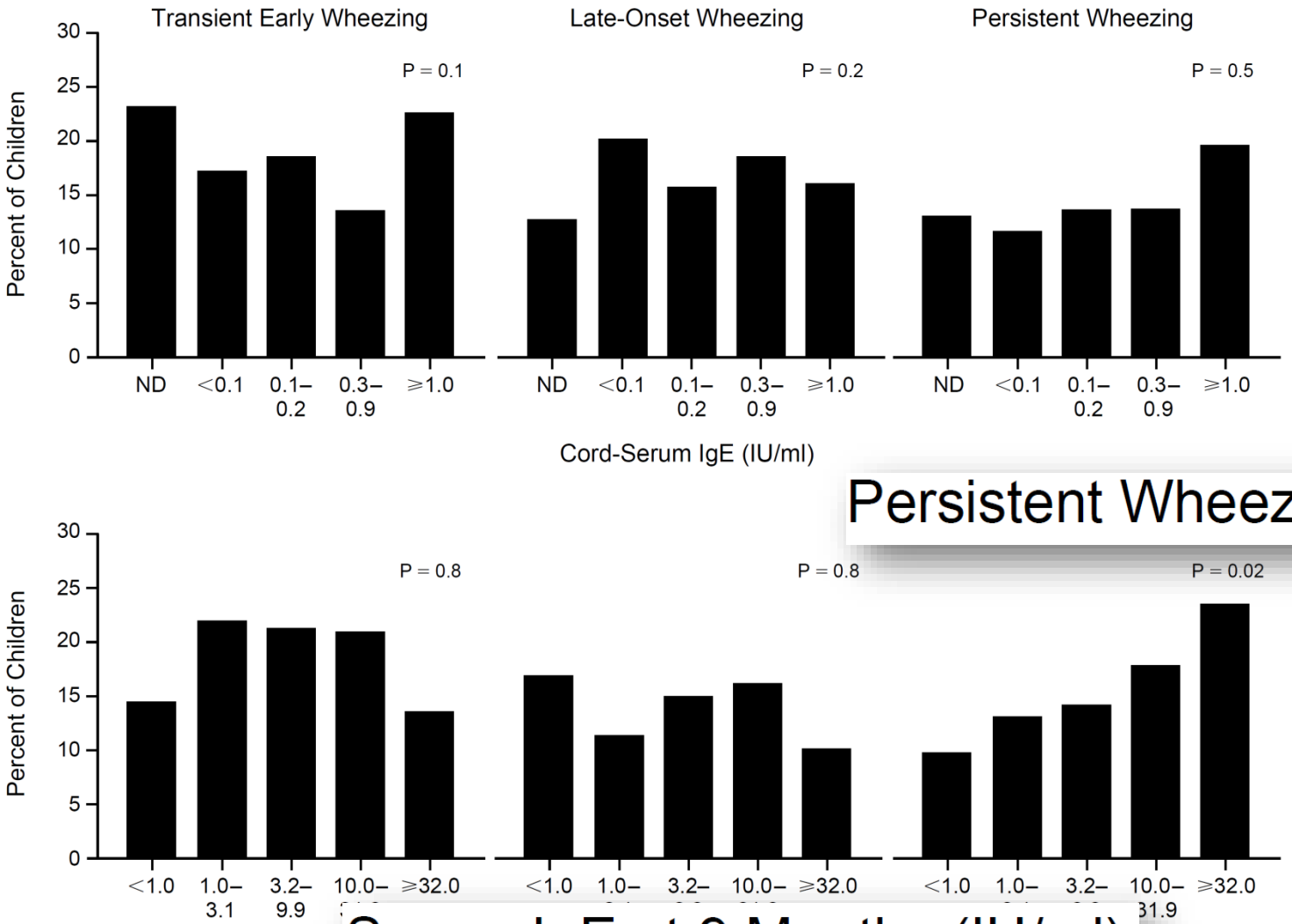
Sixty percent of children with wheezing in the first three years of life had no wheezing at six years of age. But…

Age	No Wheezing		Transient Early Wheezing	
	No.	$\dot{V}_{max}$FRC	No.	$\dot{V}_{max}$FRC
		ml/sec		*ml/sec*
<1 year	67	123.3 (110.0–138.0)	21	70.6 (52.2–93.8)†
6 years	260	1262.1 (1217.4–1308.1)	104	1097.7 (1034.9–1163.5)‡

Age	Late-Onset Wheezing		Persistent Wheezing	
	No.	$\dot{V}_{max}$FRC	No.	$\dot{V}_{max}$FRC
		ml/sec		*ml/sec*
<1 year	21	107.1 (87.5–129.6)	16	104.6 (73.6–144.5)
6 years	81	1174.9 (1111.1–1241.1)	81	1069.7 (906.9–1146.5)‡

N Engl J Med 1995;332:133-8

Serum IgE at 9mo & Persistent Wheezing



N Engl J Med 1995;332:133-8

Difference in Transient Early & Late Wheezing

Risk		Transient Early Wheezing (N = 147)	Late-Onset Wheezing (N = 112)	Persistent Wheezing (N = 100)
Eczema				
	Odds ratio (95% CI)	1.0	1.3 (0.7–2.5)	2.4 (1.3–4.6)
	Prevalence (%)	7.7	10.2	6.3	18.0
Rhinitis apart from colds				
	Odds ratio (95% CI)	1.0	1.6 (0.8–	–7.9)
	Prevalence (%)	6.7	10.2	
Maternal asthma				
	Odds ratio (95% CI)	1.0	1.5 (0.9–2.7)	1.7 (0.9–3.1)	3.0 (1.6–5.5)
	Prevalence (%)	10.7	13.6	22.0
Male sex				
	Odds ratio (95% CI)	1.0	1.0 (0.7–1.5)	2.1 (1.3–3.4)	1.9 (1.2–3.0)
	Prevalence (%)	42.7	44.2	61.6	61.0
Maternal smoking				
	Odds ratio (95% CI)	1.0	2.2 (1.3–3.7)	1.6 (0.9–2.9)	2.3 (1.2–4.4)
	Prevalence (%)	11.4	21.2	17.0	21.0

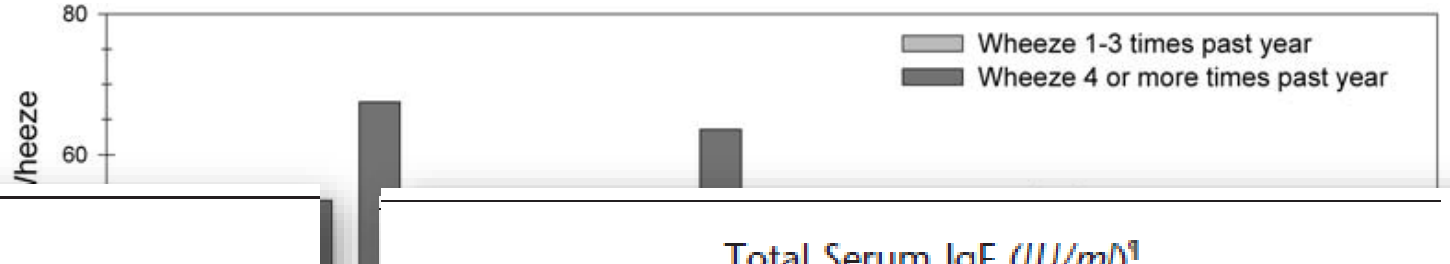
N Engl J Med 1995;332:133-8

Serum IgE, positive skin test at 6 years old

Category	Serum IgE†		Positive Skin Test	
	No. tested	Mean (95% CI)	No. tested	Prevalence
		IU/ml		%
No wheezing	222	28.1 (22.4–35.3)	317	33.8
Transient early wheezing	95	31.0 (22.3–43.1)	125	38.4
Late-onset wheezing	68	42.1 (26.6–66.0)	97	55.7‡
Persistent wheezing	75	65.6 (45.3–94.4)§	90	51.1¶
		$F = 4.94$ $P = 0.002$		$\chi^2 = 19.5$ $P < 0.001$

N Engl J Med 1995;332:133-8

Wheeze phenotype established at 6yrs old



Preschool Wheeze Phenotype*	Total Serum IgE (*IU/ml*)[¶]			
	Age 11 yr		Age 16 yr	
	n	GM (*95% CI*)	n	GM (*95% CI*)
Never wheeze	252	45 (35–57)	168	63 (49–83)
Transient early wheeze	114	56 (42–78)	74	58 (40–83)
Late-onset wheeze	83	109 (74–158)**	61	96 (66–138)
Persistent wheeze	73	93 (59–148)**	49	83 (51–132)
p Value		0.001[††]		0.2[††]

Preschool Wheeze Phenotype*	Age 11 yr		Age 16 yr		Age 11 yr		Age 16 yr	
	n	% Pos (*95% CI*)	n	% Pos (*95% CI*)	n	GM (*95% CI*)	n	GM (*95% CI*)
Never wheeze	299	51.2 (45–57)	228	68.4 (62–74)	252	45 (35–57)	168	63 (49–83)
Transient early wheeze	126	51.6 (43–61)	96	62.5 (52–72)	114	56 (42–78)	74	58 (40–83)
Late-onset wheeze	97	64.9 (55–74)[‡§]	75	78.7 (68–87)[§]	83	109 (74–158)**	61	96 (66–138)
Persistent wheeze	87	63.2 (52–73)[‡]	62	85.5 (74–93)[‡§]	73	93 (59–148)**	49	83 (51–132)
p Value		0.04[‖]		0.006[‖]		0.001[††]		0.2[††]

Am J Respir Crit Care Med Vol 172. pp 1253–1258, 2005

Wheezing and bronchial hyper-responsiveness in early childhood as predictors of newly diagnosed asthma in early adulthood: a longitudinal birth-cohort study

Debra A. Stern[1], **Wayne J. Morgan**[1,2], **Marilyn Halonen**[1], **Anne L. Wright**[1,2], and **Fernando D. Martinez**[1]

[1]Arizona Respiratory Center, University of Arizona, Tucson, Arizona

[2]Department of Pediatrics, University of Arizona, Tucson, Arizona

Healthy newborns (n=1246) in the Tucson Children's Respiratory Study

6years old; Parental characteristics early life wheezing phenotypes,
Airway function and bronchial hyperresponsiveness to cold dry air
Sensitization to *Alternaria*

22years old: Physician diagnosed asthma
Both chronic and newly diagnosed
Airway function

Lancet. 2008 September 20; 372(9643): 1058–1064

Wheezing and bronchial hyper-responsiveness in early childhood as predictors of newly diagnosed asthma in early adulthood: a longitudinal birth-cohort study

Debra A. Stern[1], **Wayne J. Morgan**[1,2], **Marilyn Halonen**[1], **Anne L. Wright**[1,2], and **Fernando D. Martinez**[1]

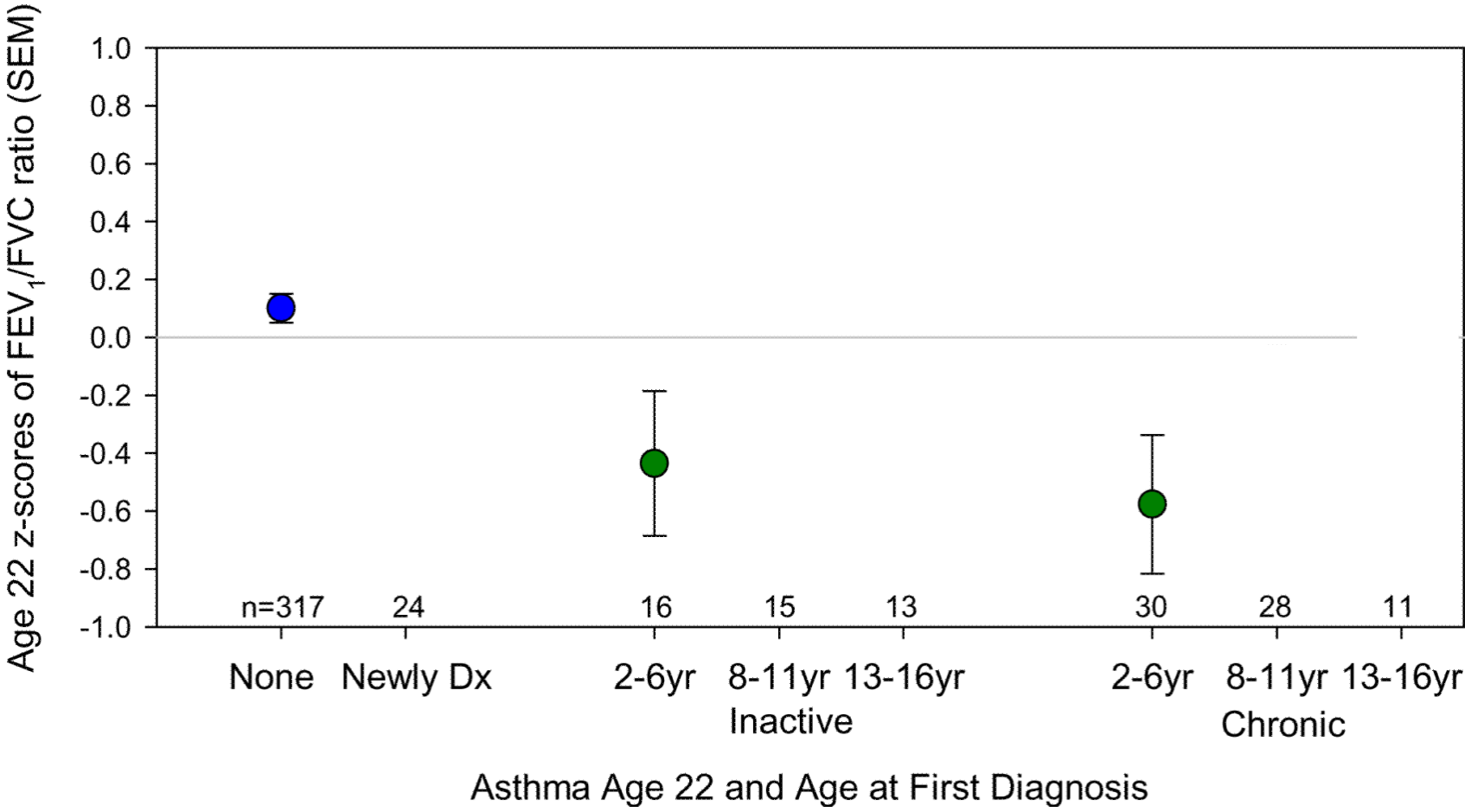
[1]Arizona Respiratory Center, University of Arizona, Tucson, Arizona

[2]Department of Pediatrics, University of Arizona, Tucson, Arizona

Physician Diagnosed Asthma and Current Symptoms		Asthma at Age 22 Years
Between 2-16 Years	at 22 Years	
-	-	No Asthma
+	-	Inactive
-	+	Newly Diagnosed
+	+	Chronic

Lancet. 2008 September 20; 372(9643): 1058–1064

Lung Function Declines in Current Asthma



Lancet. 2008 September 20; 372(9643): 1058–1064

BHR was already noted at age 6 in newly diagnosed asthma at age 22

Multinomial odds ratio for inactive, newly diagnosed, and chronic asthma at age 22 years by different risk factors in early life

Risk Factors*	Categories	Inactive			Asthma at Age 22 Years Newly Diagnosed			Chronic		
		M-OR†	(95%CI)	p	M-OR	(95%CI)	p	M-OR	(95%CI)	p
Parental asthma	Yes	2.0	1.1, 3.6	0.030	2.7	1.4, 5.2	0.004	3.2	1.9, 5.4	<0.0001
Eczema 2yr	Yes	3.8	1.9, 7.8	0.0002	1.1	0.4, 3.3	0.9	2.0	1.0, 4.1	0.047
Early	Never			ref			ref			ref
wheezing	Transient Early	1.6	0.7, 3.5	0.3	2.0	0.8, 4.8	0.14	1.4	0.7, 2.9	0.3
phenotypes	Late Onset	5.4	2.5, 11	<0.0001	4.6	1.7, 12	0.003	7.4	3.9, 14	<0.0001
	Persistent	8.9	4.0, 20	<0.0001	4.0	1.2, 14	0.027	14	6.8, 28	<0.0001
CA-BHR 6yr		2.0	1.0, 4.0	0.067	6.9	0.2, 2	0.0006	3.6	2.1, 6.4	<0.0001
		2.4	0.9, 6.5	0.083		2.3, 21		4.5	1.9, 10	0.0006
V'maxFRC quartiles 6yr	Low	1.1	0.5, 2.4	0.8	2.8	1.1, 6.9	0.029	2.1	1.1, 3.9	0.021

Lancet. 2008 September 20; 372(9643): 1058–1064

Early childhood respiratory symptoms and the subsequent diagnosis of asthma

Russell Dodge, MD, Fernando D. Martinez, MD, Martha G. Cline, MS, Michael D. Lebowitz, PhD, and Benjamin Burrows, MD *Tucson, Ariz.*

Under 5 years of age at enrollment and

A parent-administered mail survey instrument

Every 1 to 2 years for 3 to 11 years

J Allergy Clin Immunol 1996;9&48-54.

No respiratory symptom before the age of 1 year was predictive

TABLE II. Cumulative prevalence of asthma in subjects* ages 1 to 11 by symptoms before age 1

Symptom	N†	Percent with later asthma	OR (95% CI)	*p* Value
Frequent cough	12	25.0	1.6 (0.4-6.5)	0.7
No cough	129	17.1	1	
Wheeze even without colds	14	28.6	1.9 (0.5-6.9)	0.5
Wheeze only with colds	34	11.8	0.6 (0.2-2.1)	0.6
No wheeze	93	17.2	1	
Any SOBWZ	2	50.0	4.8 (0.3-80.0)	0.7
No SOBWZ	140	17.1	1	
One or more chest colds	28	21.4	1.3 (0.5-3.8)	0.7
		16.8	1	
Frequent cough, wheeze even without colds, or SOBWZ		34.8	3.2 (1.2-8.7)	<0.05‡
None of the above	119	14.3	1	

*One subject with asthma diagnosed at age 1 not included.
†Subjects in only one category for each symptom.
‡Significant when group is compared with group without symptoms.

J Allergy Clin Immunol 1996(9)48-54.

Some respiratory symptoms of the age of 1~2 year was predictive

TABLE III. Cumulative prevalence of asthma in subjects* ages 3 to 11 by symptoms at ages 1 to 2

Symptom	N†	Percent with later asthma	OR (95% CI)	*p* Value
Chronic cough	18	22.2	1.9 (0.6-6.0)	0.5
Frequent cough	30	23.3	2.0 (0.8-5.0)	0.2
No cough	344	13.1	1	
Wheeze even without colds	26	15.4	1.4 (0.5-4.3)	0.8
Wheeze only with colds	102	21.6	2.1 (1.2-3.9)	<0.05
No wheeze	261	11.5	1	
Any SOBWZ	23	30.4	2.9 (1.1-7.3)	<0.05
	371	13.2	1	
Chest colds	167	16.8	1.4 (0.8-2.5)	0.2
Frequent cough, wheeze even without colds, or SOBWZ		12.4	1	
		20.1	2.1 (1.2-3.8)	<0.01
None of the above	245	10.6	1	

J Allergy Clin Immunol 1996(9)48-54.

More respiratory symptoms of the age of 3~4 year was predictive

TABLE IV. Cumulative prevalence of asthma in subjects* ages 5 to 11 by symptoms at ages 3 to 4

Symptom	N†	Percent with later asthma	OR (95% CI)	*p* Value
Chronic cough	35	34.3	5.4 (2.4-12.0)	<0.001
	44	11.4	1.3 (0.5-3.6)	0.7
No cough	305	9.1	1	
	32	31.3	5.7 (2.4-13.5)	<0.001
Wheeze only with colds	80	16.3	2.4 (1.1-5.1)	<0.01
	269	7.4	1	
Any SOBWZ	26	42.3	7.2 (3.1-17.0)	<0.0001
	359	9.2	1	
	91	15.9	2.1 (1.1-4.0)	<0.05
One or fewer chest colds	292	9.2	1	
Chronic cough, wheeze even without colds,	68	30.9	8.5 (3.8-19.2)	<0.0001
only with colds	88	12.5	2.7 (1.1-6.7)	<0.05
More than one chest cold	29	6.9	1.4 (0.3-6.8)	0.9
			1	

Chronic cough

Wheeze even without colds

More than one chest cold

Wheeze only with colds

Any SOBWZ

Frequent cough, wheeze even without colds, or SOBWZ

*

†Subjects in only one category for each symptom.

J Allergy Clin Immunol 1996(9)48-54.

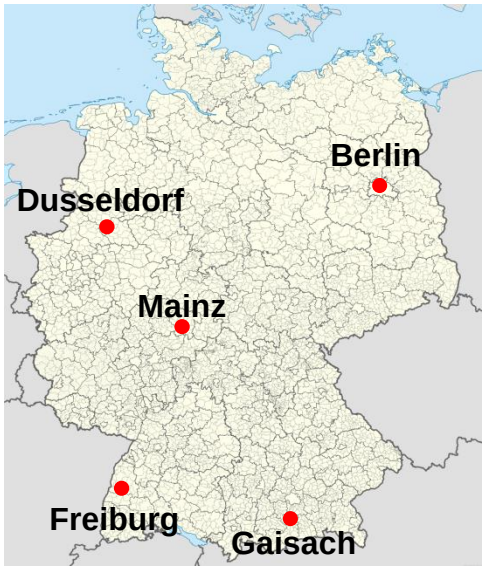
Symptoms of 3~4 year old increased risk for asthma (5~11 yrs old)

Respiratory symptoms		New asthma at ages 5-11	OR (95% CI)*	Percent with new asthma
Age 1-2	Age 3-4			
Absent (177)†	Absent (148)	8 (5.4%)	1.0	22.2
	Present (29)	10 (34.5%)‡	9.2 (3.2-26.2)	27.8
Present (96)	Absent (45)	4 (8.9%)	1.7 (0.5-6.0)	11.1
	Present (51)	14 (27.5%)	6.6 (2.6-17.0)	38.9

J Allergy Clin Immunol 1996(9)48-54.

Wheezing in childhood: incidence, longitudinal patterns and factors predicting persistence

P.M. Matricardi*, S. Illi#, C. Grüber*, T. Keil¶, R. Nickel*, U. Wahn* and S. Lau*



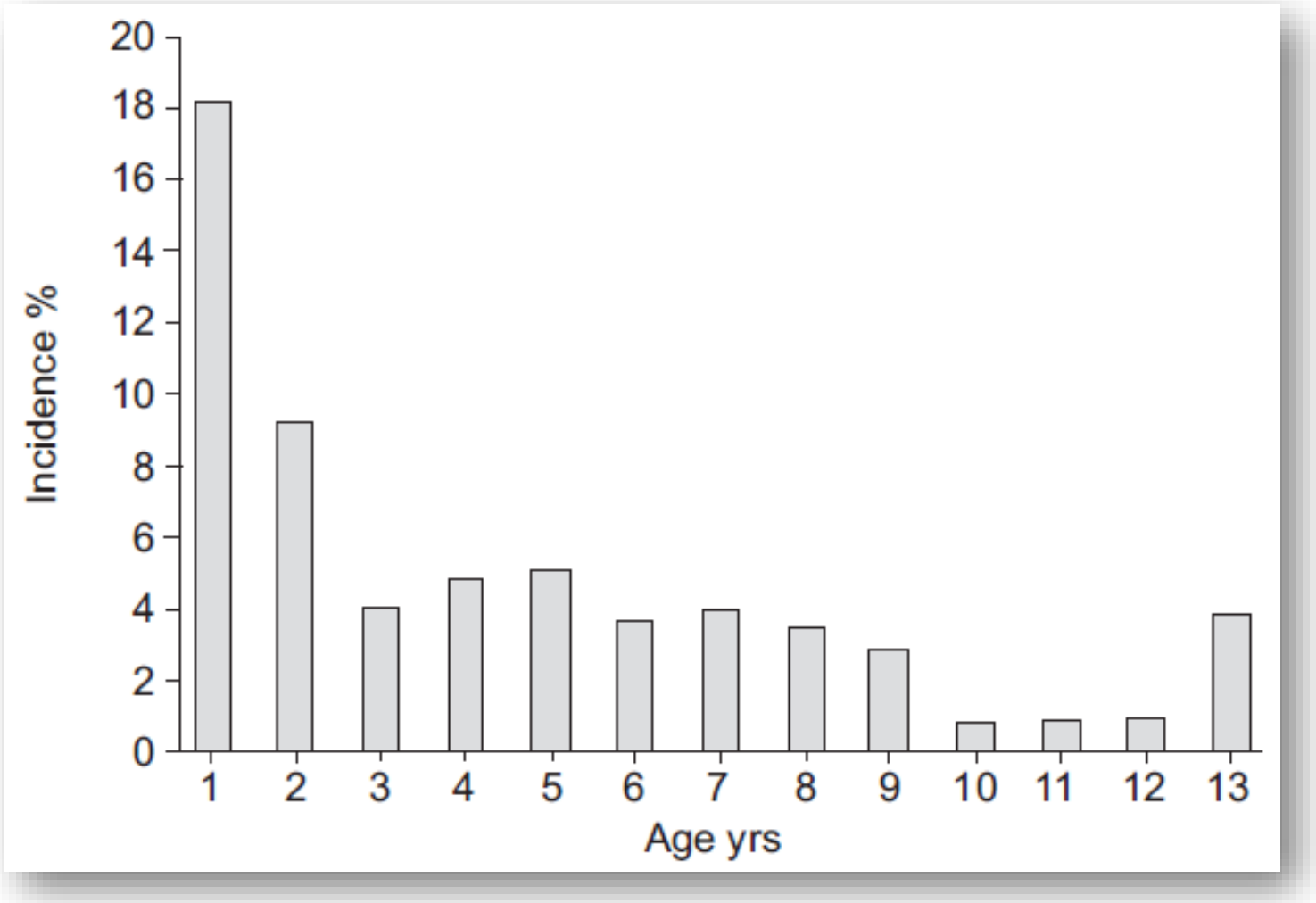
MAS 출생코호트1,314명

441명 13세까지 F/U

- Early Wheezer (첫3년 wheezing)
  - Early remittent wheezers (no wheeze 4-13yrs)
  - Early Intermittent Wheezer (not every year)
  - Early Persistent Wheezer
- Early nonwheezer (첫3년 wheezing없음)
  - Never Wheezers
  - Late Wheezers (start 3~6yrs)
  - Very Late Wheezers (start 6~yrs)

Eur Respir J 2008; 32: 585–592

Wheezing decreases over years



Eur Respir J 2008; 32: 585–592

Risk Factors: Wheezing at age 11-13 years

TABLE 3 Risk factors for wheezing at age 11–13 yrs by age at onset: results of unadjusted and adjusted[#] generalised estimation equation models

	Children with no wheeze before age 3 yrs[g]				Children with wheeze before age 3 yrs			
	OR (95% CI)	p-value	Adjusted OR[#] (95% CI)	p-value	OR (95% CI)	p-value	Adjusted OR[#] (95% CI)	p-value
Male	0.88 (0.40–1.97)	0.764			2.24 (0.91–5.47)	0.078	2.80 (1.08–7.28)	0.034
Any parental atopy	2.72 (1.12–6.61)				03–26.70)	<0.001	8.32 (2.74–25.20)	<0.001[f]
Asthma	2.42 (1.00–5.85)				05–5.94)	0.037		
Hay fever	2.67 (1.16–6				.56)	0.004		
Atopic dermatitis	0.81 (0.17–3				45)	0.059		
Any sensitisation (⩽3 yrs)	2.48 (0.95–6.44)	0.063			4.70 (1.93–11.42)	<0.001		
Food	1.57 (0.45–5.49)	0.484			2.82 (1.08–7.33)			
Perennial	–19.25)	0.024			7.44 (2.82–19.60)		41–16.09)	<0.001
Seasonal	3.31 (0.91–12.01)	0.069			3.00 (1.07–8.41)	0.037		
Elevated total IgE (3 yrs)	0.76 (0.27–2.17)	0.610			2.94 (1.03–8.41)	0.044		
Early atopic dermatitis (⩽2 yrs)	3.71 (1.51–9.13)	0.004	3.35 (1.34–8.33)	0.009	3.19 (1.32–7.71)	0.010		
High allergen exposure[¶] (⩽3 yrs)	0.47 (0.21–1.05)	0.065			1.88 (0.75–4.69)	0.176		
Interaction of sensitisation /exposure[+] (⩽3 yrs)								
No sensitisation to cat/mite[§]					1			
Sensitisation to cat/mite+ low allergen exposure[§]					6.22 (2.(			
Sensitisation to cat/mite+ high allergen exposure[§]					9.70 (2.73–34.55)	<0.001		

Any parental atopy

Any sensitisation (⩽3 yrs)

Perennial

Seasonal

Sensitisation to cat/mite+ high allergen exposure[§]

Eur Respir J 2008; 32: 585–592

The Early Course of Newly Diagnosed Asthma

Pierre Ernst, MD, MSc, Bing Cai, MSc, Lucie Blais, PhD, Samy Suissa, PhD

A cohort of 13,671 patients in Saskatchewan, Canada,

Initially 5 and 44 years.

Followed prospectively,

The intensity of asthma therapy was measured during successive 12-month periods.

AmJ Med. 2002;112:44–48

Treatment waned over time

a cohort of 13,671 patients in Saskatchewan, Canada
5~44 years old

Characteristics	Mild (n = 6661)	Intermediate (n = 6033)	Severe (n = 977)	All (n = 13 671)
	Number (%) or Mean ± SD			
Follow-up (years)	4.3 ± 2.2	4.0 ± 2.1	3.8 ± 2.0	4.1 ± 2.2
Age at entry (years)	19.3 ± 11.4	21.0 ± 11.9	23 ± 12.7	20.3 ± 11.8
<15 years	3191 (47.9)	2492 (41.3)	360 (36.8)	6043 (44.2)
Male sex	3437 (51.6)	3095 (51.3)	496 (50.8)	7027 (51.4)
Cohort entry				
1975–1987	5082 (76.3)	3451 (57.2)	640 (65.5)	9173 (67.1)
1988–1993	1579 (23.7)	2582 (42.8)	337 (34.5)	4498 (32.9)

Am J Med. 2002;112:44–48

Symptom decreased during five-year follow up

Table 2. Number and Cumulative Rates of Changes in Treatment Intensity during 3 and 5 Years of Follow-up, Stratified by Age at Entry (<15 Years Old versus ≥ 15 Years Old)

Change in Treatment Intensity	Number of Patients at Baseline	3-Year Follow-up n (Rate/100 Patients)	3-Year Follow-up *P* Value*	5-Year Follow-up n (Rate/100 Patients)	5-Year Follow-up *P* Value*
Mild to severe					
<15 years old	3187	48 (1.9)	0.61	64 (3.3)	0.61
=15 years old	3474	47 (1.7)		64 (2.9)	
Severe to not severe					
<15 years old	359	244 (78.4)	<0.001	246 (80.0)	<0.001
≥15 years old	618	318 (57.7)		325 (61.2)	
Severe to mild					
<15 years old	359	66 (23)	<0.001	73 (34)	<0.001
≥15 years old	618	54 (10)		59 (13)	0.03
Severe to remission					
<15 years old	359	51 (16)	0.07	56 (23)	0.03
≥15 years old	618	63 (12)		66 (14)	

AmJ Med. 2002;112:44–48

Sex-specific risk factors for childhood wheeze and longitudinal phenotypes of wheeze

Sze Man Tse, MDCM, MPH,[a] Sheryl L. Rifas-Shiman, MPH,[b] Brent A. Coull, PhD,[c] Augusto A. Litonjua, MD, MPH,[d] Emily Oken, MD, MPH,[b] and Diane R. Gold, MD, MPH[d] *Montreal, Quebec, Canada, and Boston, Mass*

a prospective prebirth cohort study

2128 singleton live-born infants

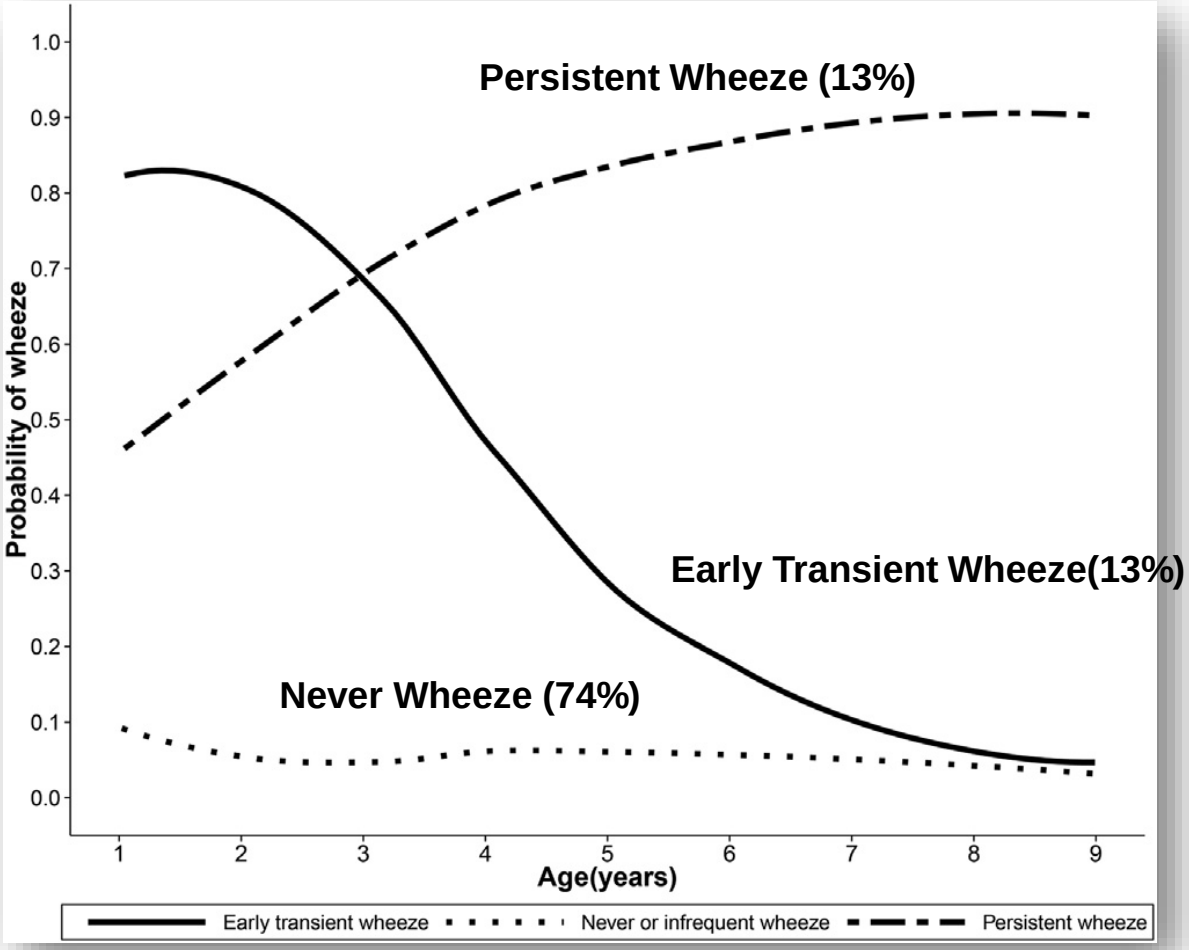
in-person visits and on mailed questionnaires,

mothers were invited to respond to a questionnaire about the child's health at birth, 6 months and 1 year of age, and approximately 1-year intervals thereafter

J Allergy Clin Immunol 2016;138:1561-8

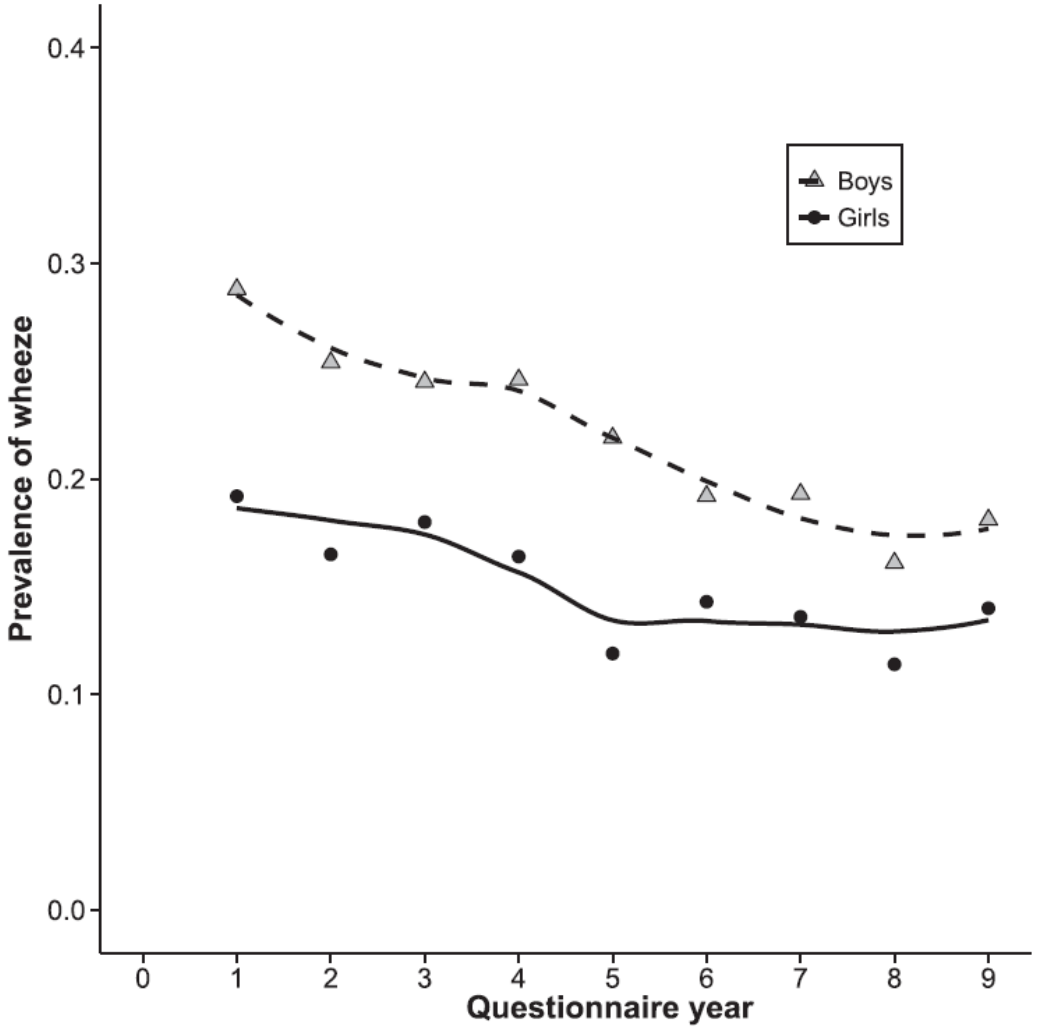
Sex-specific risk factors for childhood wheeze and longitudinal phenotypes of wheeze

Sze Man Tse, MDCM, MPH,[a] Sheryl L. Rifas-Shiman, MPH,[b] Brent A. Coull, PhD,[c] Augusto A. Litonjua, MD, MPH,[d] Emily Oken, MD, MPH,[b] and Diane R. Gold, MD, MPH[d] *Montreal, Quebec, Canada, and Boston, Mass*



J Allergy Clin Immunol 2016;138:1561-8

Wheezing decreases over years



J Allergy Clin Immunol 2016;138:1561-8

Risk Factor: Parental Asthma, Bronchiolitis before 1yr old

TABLE IV. Multinomial logistic regression for wheeze phenotypes stratified by sex (vs never/infrequent wheeze)*

	Early transient wheeze		Persistent wheeze	
	Girls (n = 64)	Boys (n = 101)	Girls (n = 69)	Boys (n = 101)
Maternal asthma	2.03 (0.97-4.25)	3.59 (1.90-6.75)	2.13 (1.04-4.35)	[illegible]
	1.29 (0.59-2.83)	0.85 (0.35-2.09)	1.46 (0.68-3.15)	[illegible]
Household income >$70,000/y	0.78 (0.42-1.46)	0.85 (0.48-1.50)	0.72 (0.38-1.36)	0.72 (0.41-1.26)
Child race/ethnicity (vs white)				
Black*	0.56 (0.21-1.53)	1.25 (0.57-2.76)	3.23 [illegible]	
Hispanic	0.69 (0.13-3.59)	1.11 (0.35-3.53)	3.60 [illegible]	[illegible]
Other	0.83 (0.38-1.82)	1.27 (0.64-2.51)	1.39 (0.63-3.11)	0.96 (0.46-2.01)
Season of birth (vs winter)				
Spring	0.93 (0.46-1.88)	1.74 (0.88-3.43)	0.98 (0.46-2.09)	0.87 (0.45-1.69)
Summer	0.54 (0.25-1.19)	1.36 (0.69-2.70)	0.85 (0.40-1.84)	0.82 (0.43-1.57)
Fall	0.52 (0.23-1.19)	1.30 (0.63-2.70)	0.67 (0.30-1.52)	0.86 (0.44-1.70)
Gestation length (wk)	0.93 (0.81-1.07)	1.05 (0.91-1.21)	0.97 (0.84-1.12)	0.92 (0.81-1.04)
Bronchiolitis before age 1 y	[illegible]5-1.03)	1.13 (0.87-1.47)	0.83 (0.61-1.13)	1.11 (0.86-1.42)
	[illegible]6-0.98)	0.98 (0.92-1.03)	0.97 (0.91-1.03)	1.02 (0.97-1.08)
Environmental smoke exposure before age 1 y	1.73 (0.67-4.44)	1.02 (0.39-2.64)	1.96 (0.81-4.73)	2.16 (0.96-4.89)
Bronchiolitis before age 1 y	4.84 (2.34-9.98)	10.17 (5.47-18.93)	4.38 (2.03-9.45)	6.49 (3.29-12.79)
Atopic dermatitis before age 1 y	2.06 (1.04-4.09)	1.24 (0.69-2.23)	2.88 (1.54-5.38)	2.01 (1.16-3.49)

*Statistically significant interaction with sex on persistent wheeze.

Boys

Paternal asthma

J Allergy Clin Immunol 2016;138:1561-8

Remission and Persistence of Asthma Followed From 7 to 19 Years of Age

AUTHORS: Martin Andersson, MD,[a,b] Linnea Hedman, PhD,[a] Anders Bjerg, MD, PhD,[a,c] Bertil Forsberg, PhD,[b] Bo Lundbäck, MD, PhD,[a,c] and Eva Rönmark, PhD[a,b]

[a]*The OLIN Studies, Norrbotten County Council, Luleå, Sweden;* [b]*Occupational and Environmental Medicine, Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden; and* [c]*Krefting Research Centre, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden*

KEY WORDS
adolescence, asthma, longitudinal, remission, sensitization

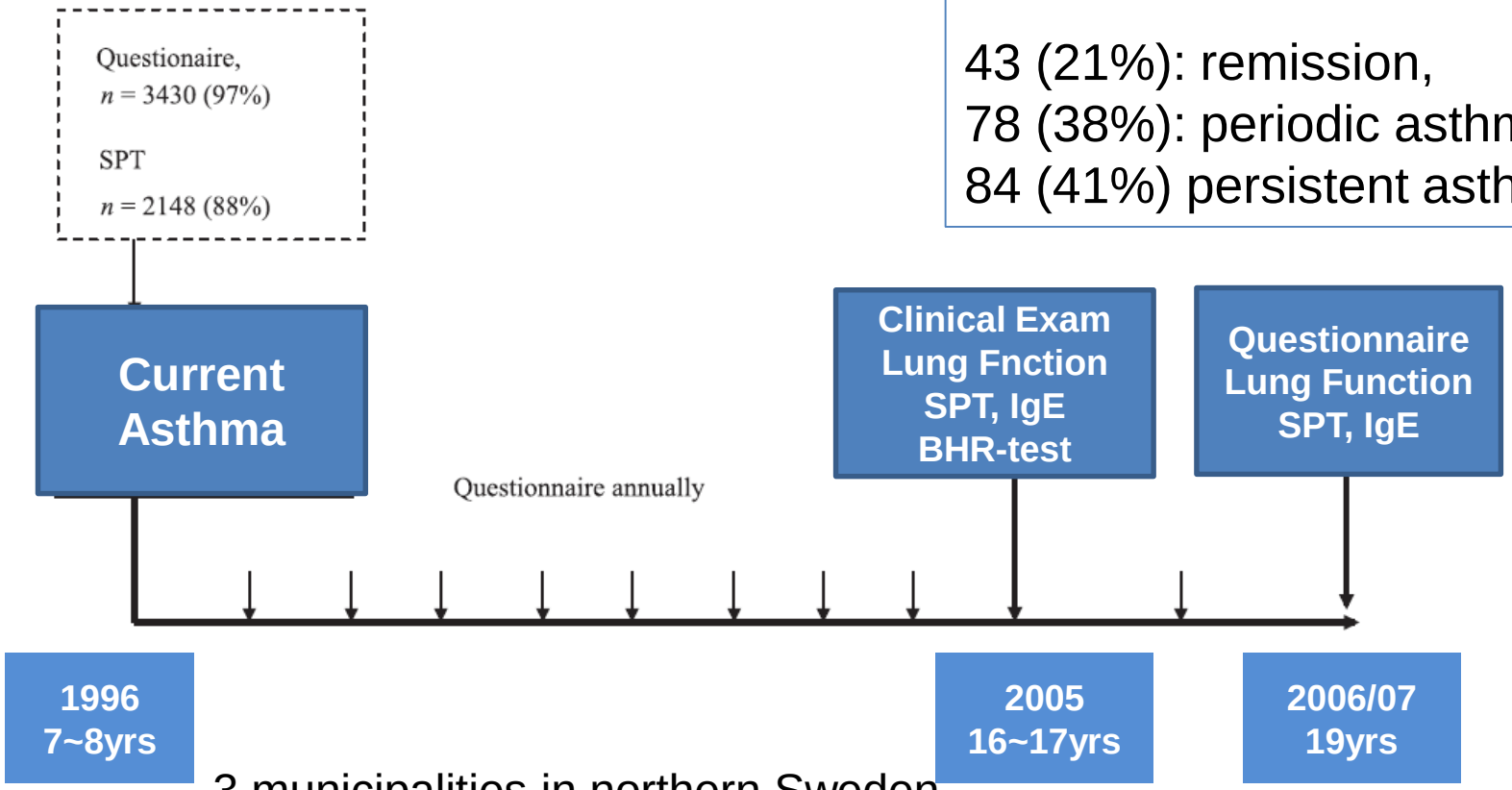
ABBREVIATIONS

WHAT'S KNOWN ON THIS SUBJECT: The natural history of asthma during adolescence is dynamic because both remission and relapse are common. Remission has consistently been associated with mild asthma and the absence of sensitization.

WHAT THIS STUDY ADDS: One in 5 children with asthma remitted from age 7 to 19. Remission was defined as no wheezing and no medication for ≥3 years and was inversely related to female gender, sensitization to furred animals, and asthma severity at baseline.

Of 205 subjects at age 19,

43 (21%): remission,
78 (38%): periodic asthma,
84 (41%) persistent asthma.



3 municipalities in northern Sweden

Pediatrics 2013;132:e435–e442

Phenotype at age 7~8yrs to progress persistent Asthma at 19yrs

TABLE 1 Prevalence (%) of Baseline Characteristics at Age 7 to 8 Years Among the Entire Cohort, Among All Participants at Endpoint (19 Years), and by

Positive SPT[b]

Physician-diagnosed rhinitis

Physician-diagnosed eczema

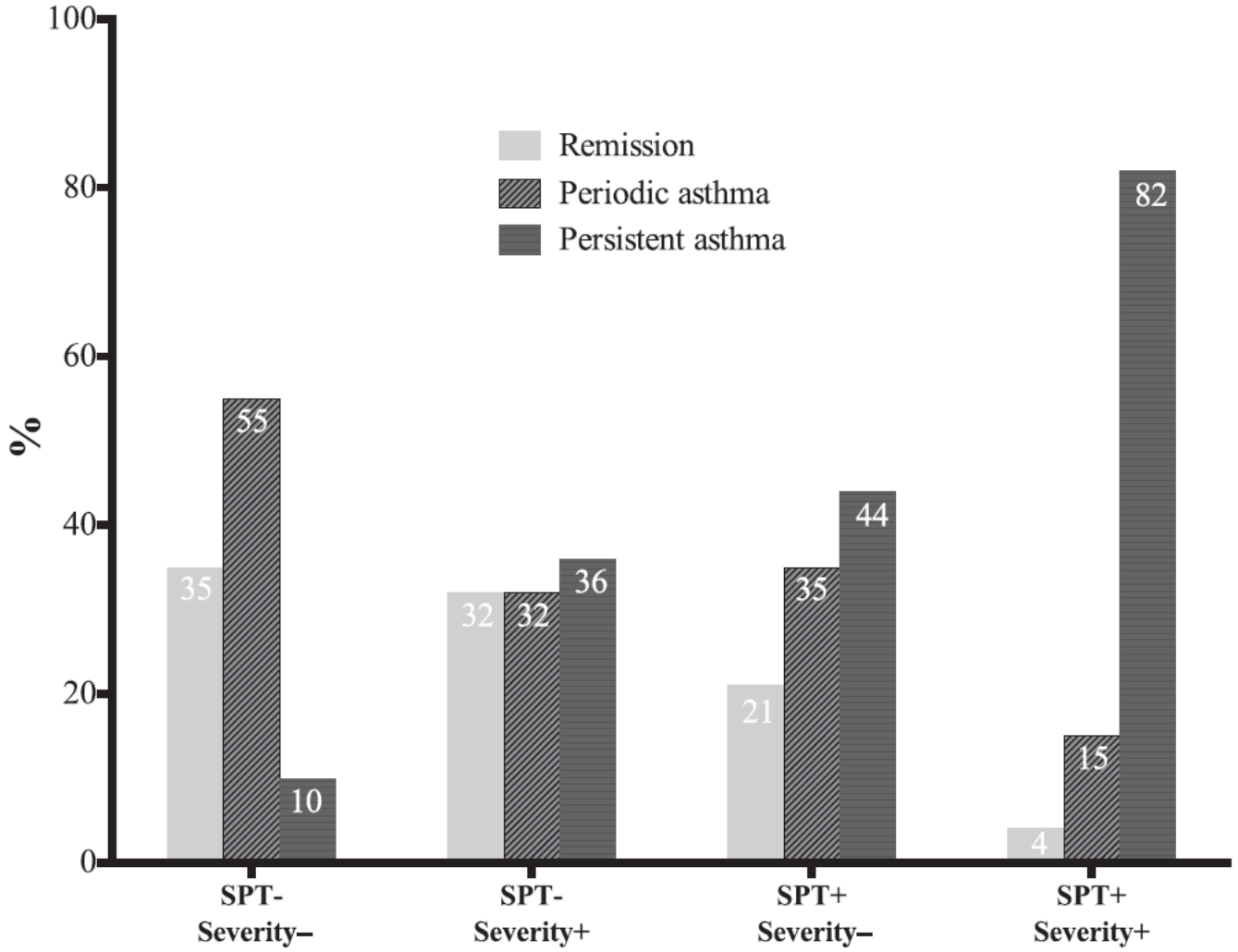
Asthma score ≥2 of 5

Current ICS use

			Participants at Endpoint			
		= 205)	Persistent Asthma ($n = 84$)	Periodic Asthma ($n = 78$)	Remission ($n = 43$)	P^a
		78/146)	77% (44/57)	39% (21/54)	37% (13/35)	<.001
		71/205)	49% (41/84)	26% (20/78)	23% (10/43)	.002
		71/205)	50% (42/84)	24% (19/78)	23% (10/43)	.001
		67/205)	49% (41/84)	22% (17/78)	21% (9/43)	<.001
		102/205)	68% (57/84)	44% (34/78)	26% (11/43)	<.001
Male gender	58% (143/248)	58% (118/205)	55% (46/84)	53% (41/78)	72% (31/43)	.091
Asthma in the family	40% (100/248)	40% (82/205)	44% (37/84)	36% (28/78)	40% (17/43)	.570
Rural living	32% (75/233)	29% (57/194)	32% (25/79)	29% (22/75)	25% (10/40)	.754
Mother smoked during pregnancy			28% (22/79)	45% (34/75)	38% (16/42)	.078
			18% (15/82)	33% (26/78)	37% (16/43)	.035
Self-reported traffic exposure	32% (77/241)	30% (60/198)	24% (19/80)	36% (27/76)	33% (14/42)	.248
Ever dampness at home	30% (71/240)	26% (52/199)	23% (18/80)	25% (19/76)	35% (15/43)	.316
Living in an apartment	28% (63/229)	23% (45/192)	17% (13/79)	34% (24/71)	19% (8/42)	.033

Pediatrics 2013;132:e435–e442

Severity and Skin Prick Tests decides the Prognosis



Pediatrics 2013;132:e435–e442

Positive SPT to animal was associated with Persistence

TABLE 2 Prevalence (%) of Allergic Sensitization at Age 7 to 8 Years by Persistent, Periodic, and Remitted Asthma at Age 19 Years

	Persistent Asthma (n = 57)	Periodic Asthma (n = 54)	Remission (n = 35)	P[a]
Any positive SPT pollen	46% (25/55)	20% (11/54)	29% (10/35)	.017
Positive SPT birch	38% (21/55)	19% (10/54)	20% (7/35)	.041
Any positive SPT animals	12/53)	11% (6/54)	17% (6/35)	<.001
Positive SPT cat	3/52)	2% (1/53)	3% (1/34)	
Positive SPT horse	41/55)	35% (19/54)	29% (10/35	<.001
Positive SPT dog	37/55)	32% (17/54)	26% (9/35)	.005
	24/54)	24% (13/54)	14% (5/35)	
	29/55)	26% (14/54)	18% (6/34)	.001
Any positive SPT molds	10/54)	2% (1/53)	6% (2/33)	
Any positive SPT mites	8% (4/53)	0% (0/53)	6% (2/33)	.137

Pediatrics 2013;132:e435–e442

High-titer IgE to animals were strongly associated with asthma

TABLE I. Univariable analysis of asthma based on a physician's diagnosis for different levels of IgE antibodies to inhalant allergens

	IgE titer by class in students with or without* asthma†			Odds ratios for asthma (based on phys		
		Class 1-3	Class 4-6	Any IgE antibody, >0.35 IU/mL (≥class 1)	IgE antibody 0.36-17.5 IU/mL (class 1-	
Cat dander		46/119	23/31	3.8 (2.6-5.5)‡	3.2 (2.1-4.8)‡	4.6 (2.6-8.2)‡
Dog dander		45/115	21/10	4.4 (3.0-6.4)‡	3.2 (2.1-4.9)‡	13.2 (6.1-28.7)‡
Dog epithelium		26/46	7/5	4.3 (2.6-6.9)‡	3.7 (2.2-6.2)‡	8.0 (2.5-25.5)‡
Horse		35/81	13/13	3.6 (2.4-5.5)‡	3.1 (2.0-4.8)‡	5.9 (2.7-13.0)‡
Any mammal		45/128	34/40	4.3 (3.0-6.2)‡	3.2 (2.1-4.9)‡	5.7 (3.5-9.4)‡
		12/63	0/0	1.0 (0.5-2.0), $P = .88$	1.0 (0.5-2.0), $P = .88$	—
Alternaria species	145/803	4/11	0/0	2.0 (0.6-6.4), $P = .27$	2.0 (0.6-6.4), $P = .27$	—
Birch tree	89/661	40/107	20/46	2.9 (2.0-4.2)‡	2.8 (1.8-4.2)‡	2.6 (1.5-4.5)‡
Timothy grass	97/647	37/115	15/52	2.1 (1.4-3.0)‡	2.1 (1.4-3.3)‡	1.6 (0.9-3.0), $P = .10$

*Numbers before and after the forward slash indicate students with and without asthma, respectively.
†As indicated by a physician's diagnosis of asthma.
‡$P < .001$.

3 municipalities in northern Sweden

J Allergy Clin Immunol 2016;138:1582-90

Demographic and clinical characteristics of children and adolescents with severe or difficult-to-treat asthma

Bradley E. Chipps, MD,[a] Stanley J. Szefler, MD,[b] F. Estelle R. Simons, MD,[c] Tmirah Haselkorn, PhD,[d] David R. Mink, MS,[e] Yamo Deniz, MD,[d] and June H. Lee, MD,[d] for the TENOR Study Group* *Sacramento and South San Francisco, Calif, Denver, Colo, and Winnipeg, Manitoba, Canada*

The TENOR study

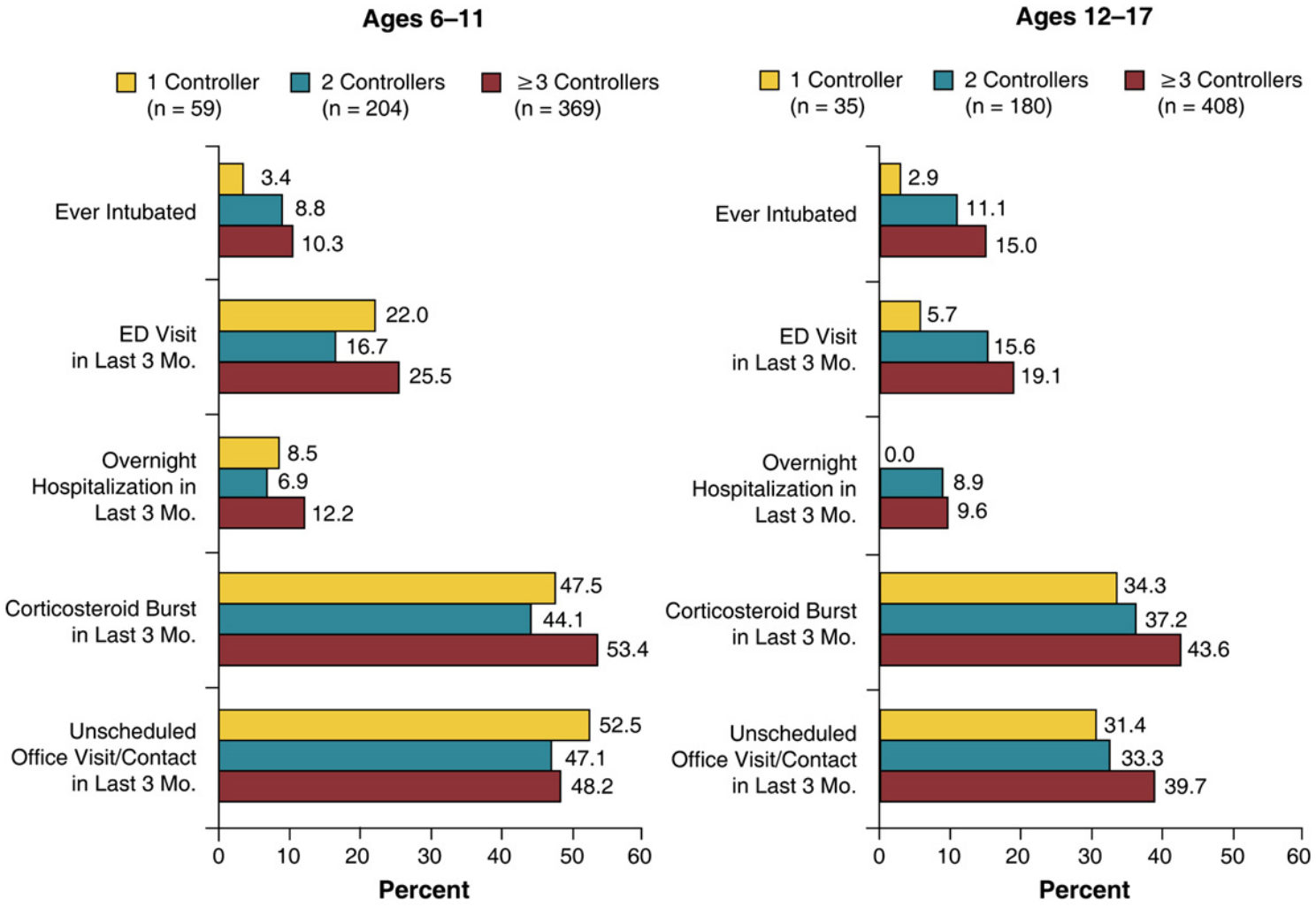
A prospective, observational, 3-year study (2001-2004)

Patients with **severe or difficult-to-treat asthma** who received care from either an allergist or a pulmonologist.

6~17 years old

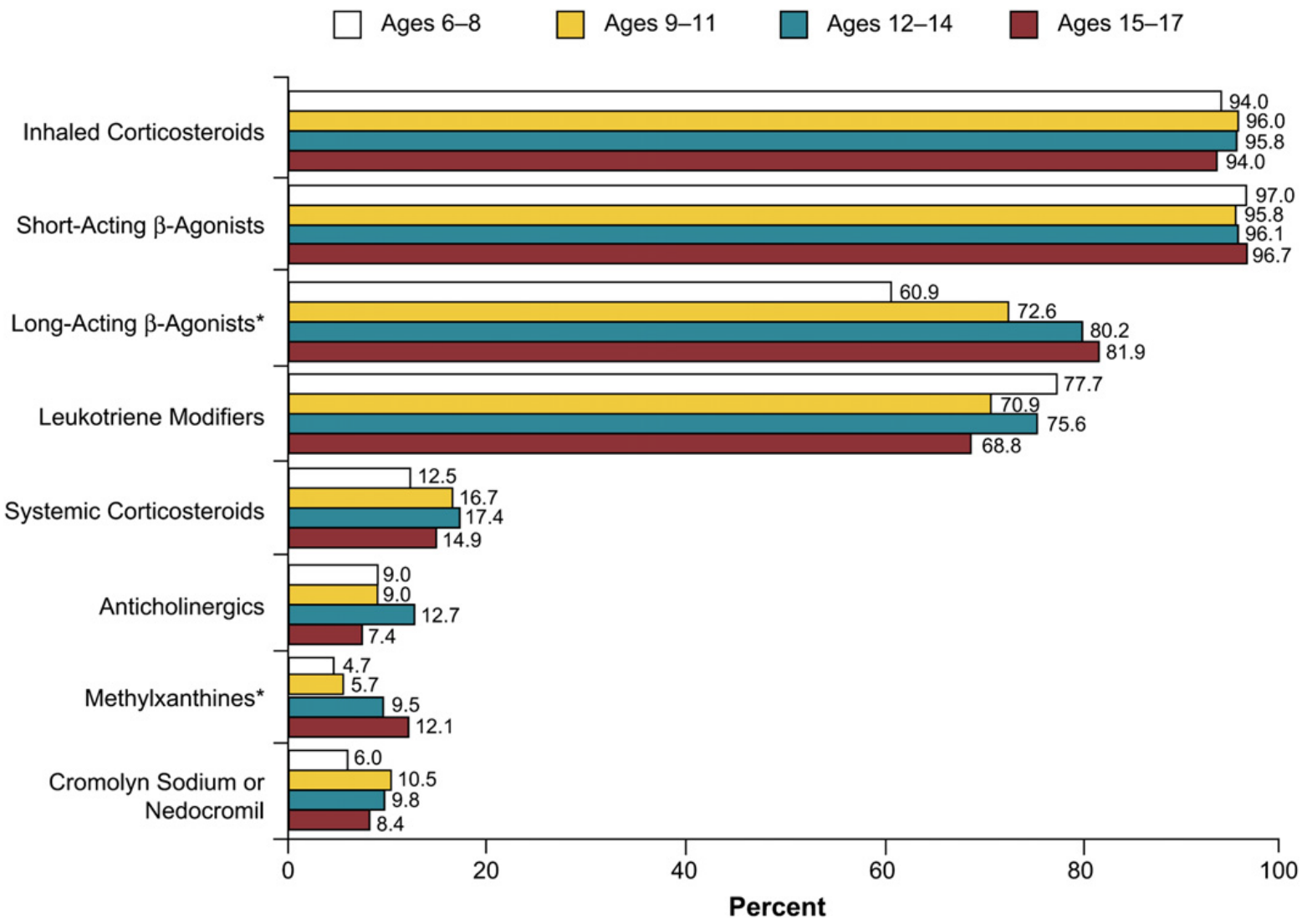
J Allergy Clin Immunol 2007;119:1156-63

Health care utilization by long term controller in Severe Asthma



J Allergy Clin Immunol 2007;119:1156-63

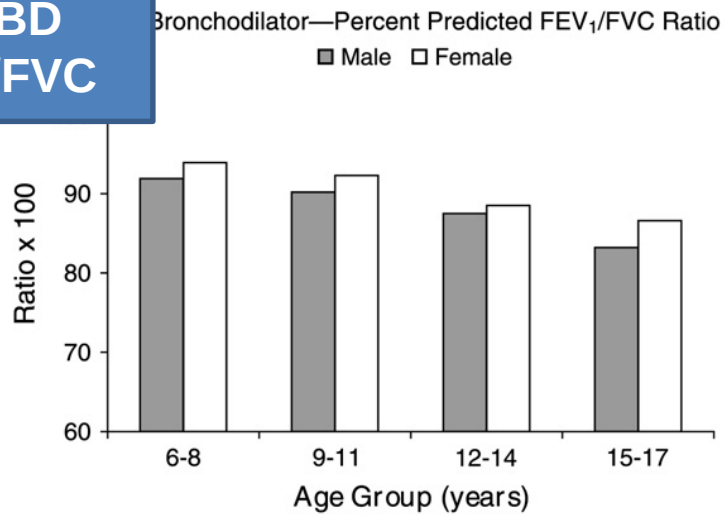
Multiple Medication in Severe Asthma



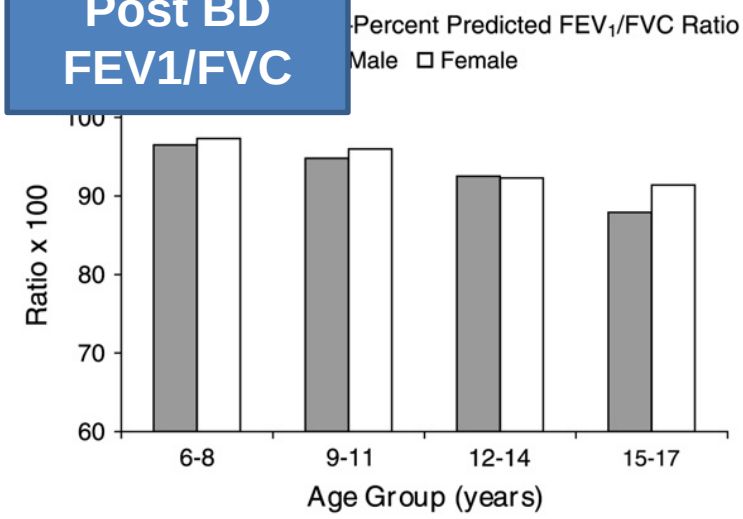
J Allergy Clin Immunol 2007;119:1156-63

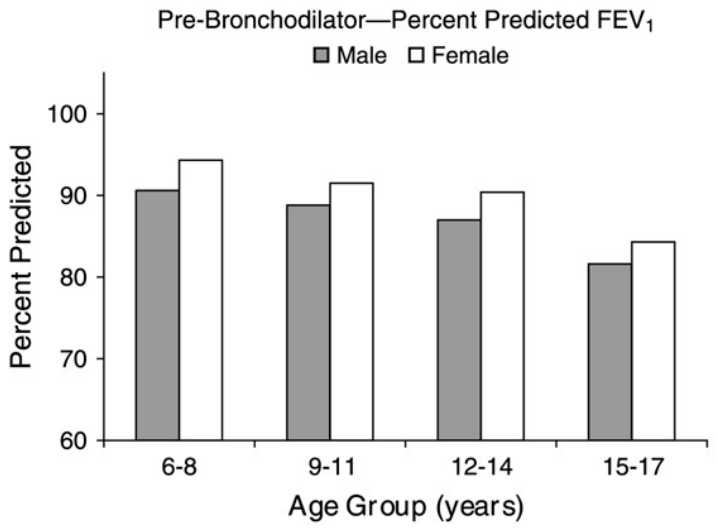
Lung Function Decline despite of multiple treatment

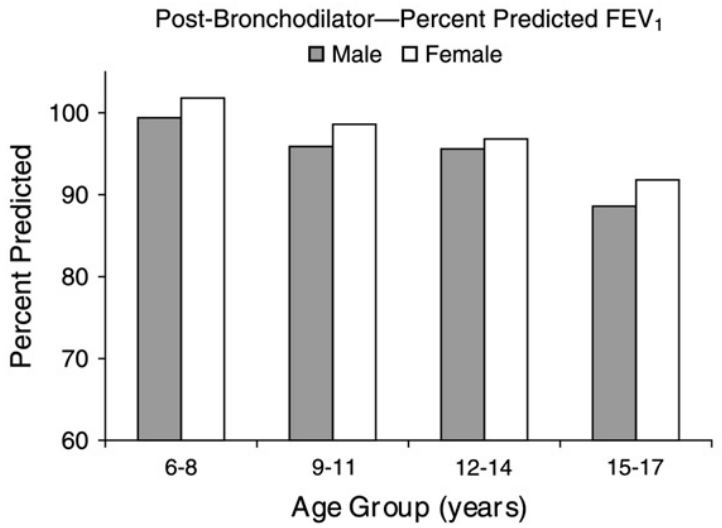
Pre BD FEV1/FVC



Post BD FEV1/FVC







J Allergy Clin Immunol 2007;119:1156-63

Childhood factors associated with asthma remission after 30 year follow up

J M Vonk, D S Postma, H M Boezen, M H Grol, J P Schouten, G H Koëter, J Gerritsen

Thorax 2004;**59**:925–929. doi: 10.1136/thx.2003.016246

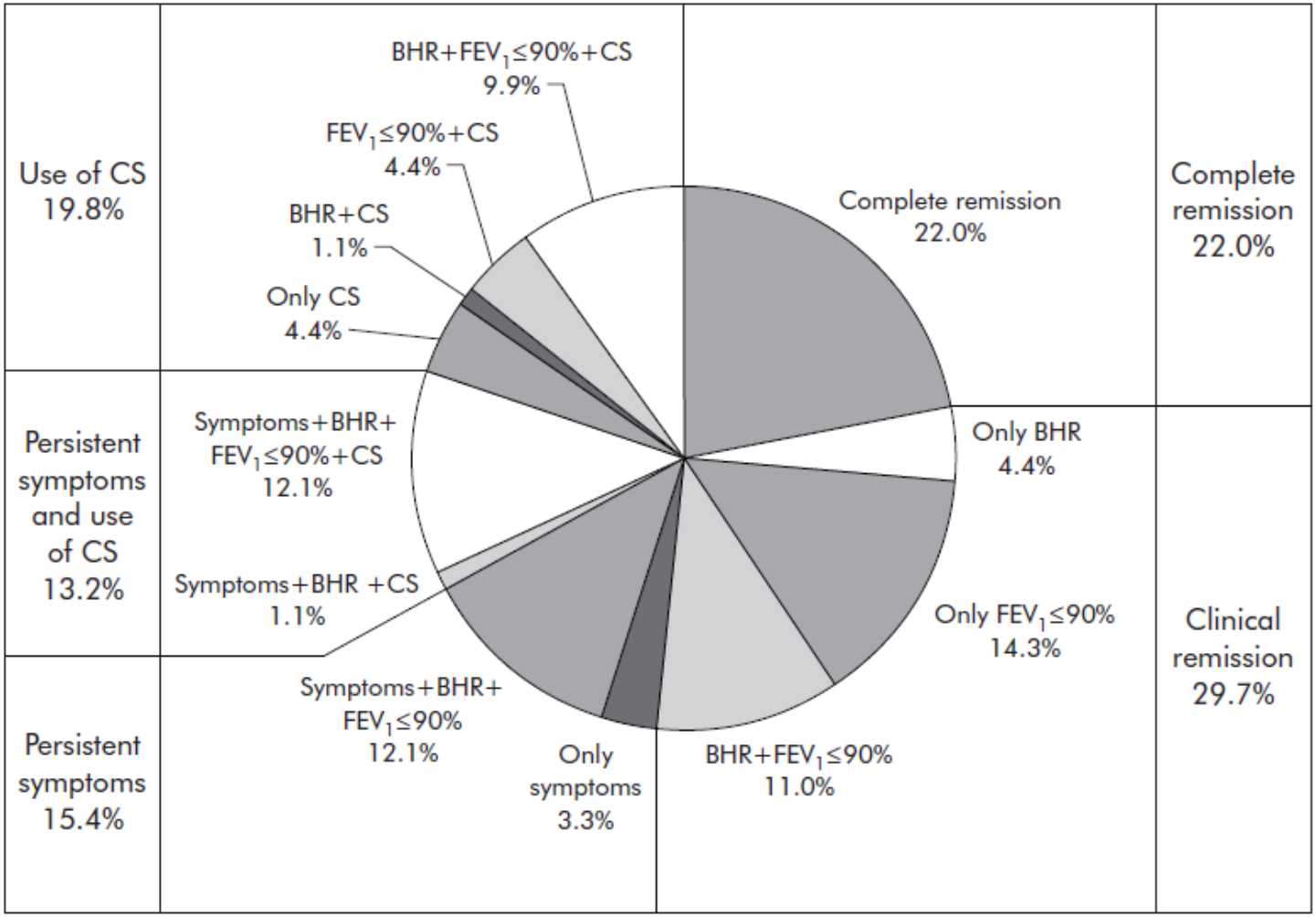
119 allergic asthmatic children
outpatient clinic of the pediatric pulmonology department of the University Hospital of Groningen

1. 1966 ~1969 (visit 1, age 5–14 years)
2. 1983 ~1986 (visit 2, age 21–33 years)
3. 1995 and 1996 (visit 3, age 32–42 years)

Complete Remission
Sx (-), no ICS use, normal lung function (FEV_1>90%), no BHR (PC_{10}>16mg/ml)

Thorax 2004;59:925–929

Complete remission 22%, Clinical Remission 30%



Thorax 2004;59:925–929

Good Lung Function and Lung Function Improvement

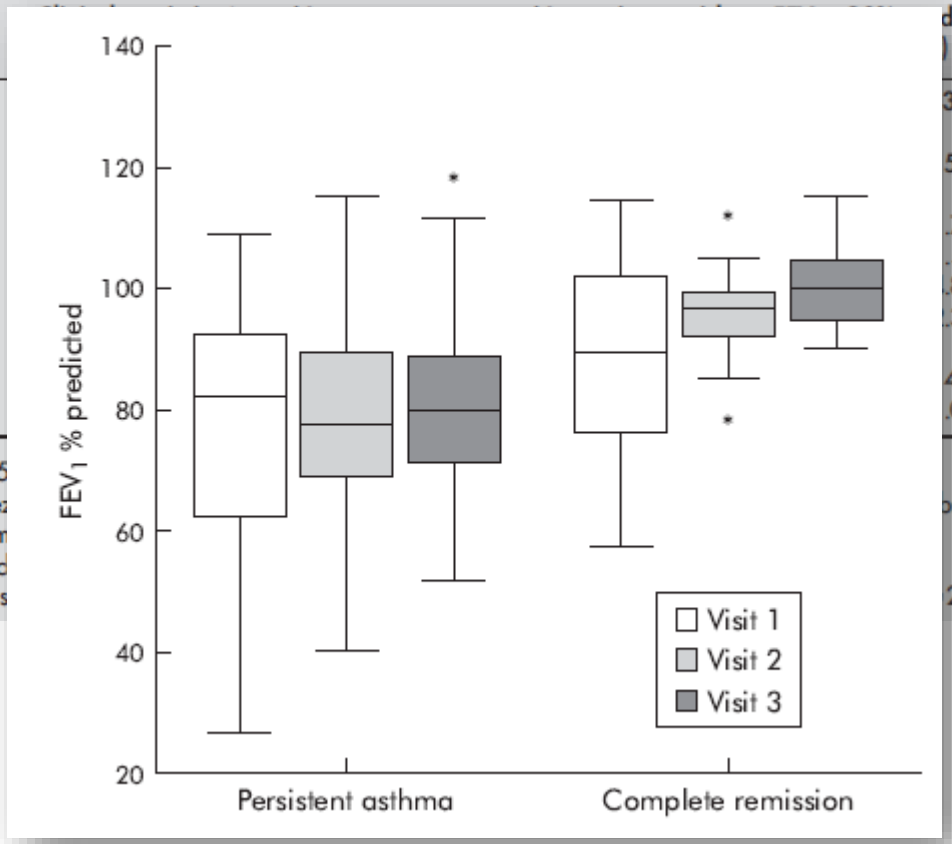
Table 2 Multiple logistic regression analyses on complete and clinical remission of asthma† at visit 3, on no symptoms‡ at visit 3, on no use of corticosteroids at visit 3, on FEV_1 >90% predicted at visit 3, and on no BHR at visit 3 (n=75)

	Complete remission* (n=15 v n=60)		No BHR (n=34 v n=41)	
FEV1%pred visit 1 (per 10%)		57)	34.78)	1.85 (1.08 to 3.17)
visit 1 (per 10%)		51)	5.31)	1.34 (0.88 to 2.03)
FEV1% pred visit 2 – visit 1 (per 10%)		00)	.70)	2.34 (0.67 to 8.17)
		54)	.53)	1.00 (0.74 to 1.37)
		19)	.86)	0.65 (0.20 to 2.13)
		77)	.38)	**0.26 (0.08 to 0.87)**
		.46)	4.19)	0.83 (0.26 to 2.73)
Pack years visit 3	1.00 (0.94 to 1.07)		.07)	1.03 (0.98 to 1.09)

Values are presented as odds ratios with 95
*Complete remission: no symptoms of whee
remission: no symptoms of wheeze or asthm
†Symptoms of wheeze and/or asthma attac
‡Eosinophilia: 0–5 years: ≥500 × 10^6 cells

…sence of BHR. Clinical

… 250 × 10^6 cells/l.



Thorax 2004;59:925–929

Current reviews of allergy and clinical immunology
(Supported by a grant from Glaxo Wellcome, Inc, Research Triangle Park, NC)
Series editor: Harold S. Nelson, MD

The Melbourne Asthma Study: 1964-1999

Peter D. Phelan, MD, FRACP, Colin F. Robertson, MD, MSc, FRACP, and Anthony Olinsky, MB, BCh, FCPSA, FRACP *Melbourne, Australia*

- Randomly selected from the Melbourne community at the age of 7 years in 1964
- These subjects have been followed prospectively at 7-year intervals, with the last review in 1999, when their average age was 42 years

J Allergy Clin Immunol 2002; 109:189

Current reviews of allergy and clinical immunology
(Supported by a grant from Glaxo Wellcome, Inc, Research Triangle Park, NC)
Series editor: Harold S. Nelson, MD

The Melbourne Asthma Study: 1964-1999

Peter D. Phelan, MD, FRACP, Colin F. Robertson, MD, MSc, FRACP, and
Anthony Olinsky, MB, BCh, FCPSA, FRACP *Melbourne, Australia*

- **Control** group: 105 children who had never wheezed;

- **Mild wheezy bronchitis** group: 74 children with fewer than 5 episodes of wheezing associated with bronchitis or respiratory tract infection;

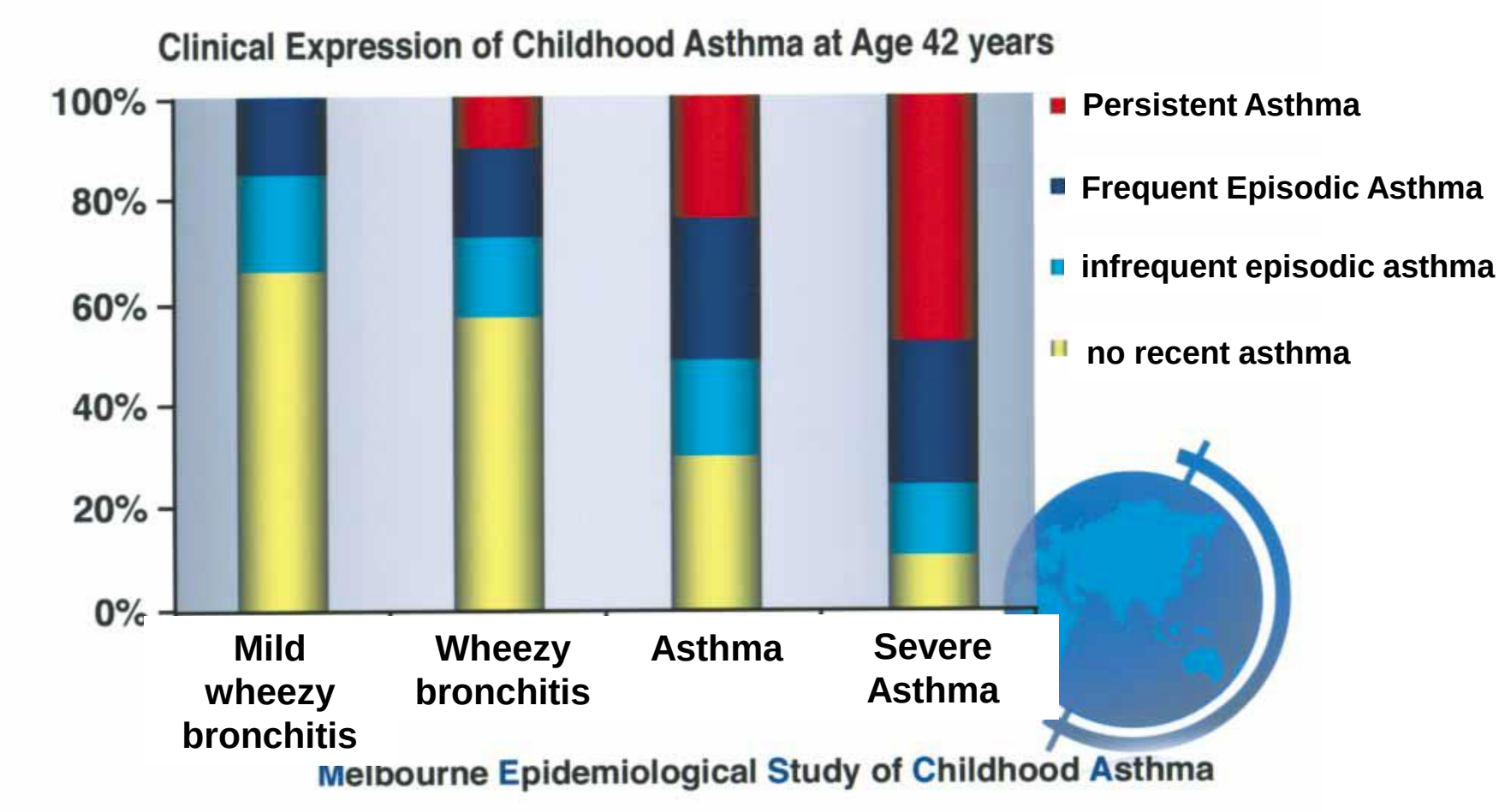
- **Wheezy bronchitis** group: 104 children with 5 or more episodes of wheezing associated with bronchitis or respiratory tract infection;

- **Asthma** group: 113 children with wheezing unassociated with respiratory tract infection

- **Severe asthma** group: 83 children with onset of symptoms before 3 years of age, persistent symptoms at 10 years of age, barrel-chest deformity, reduction of FEV1/forced vital capacity to 50% or less, or some combination of these factors.

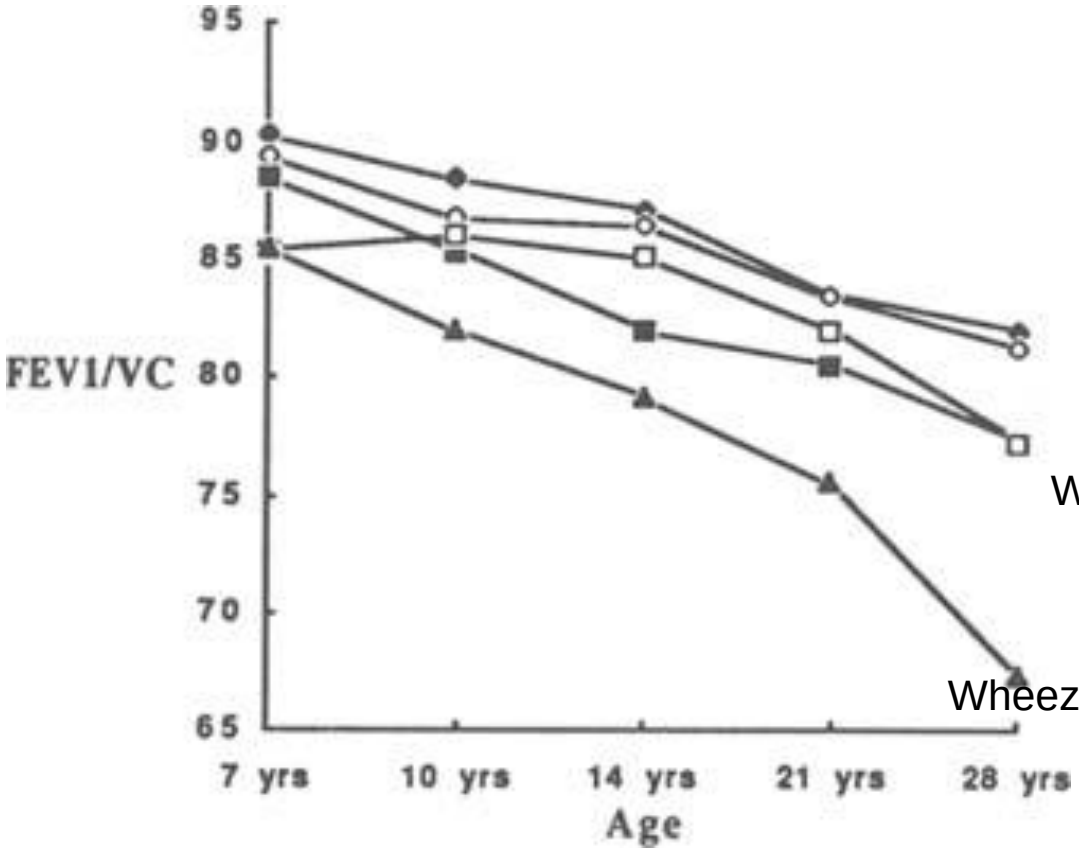
J Allergy Clin Immunol 2002; 109:189

Asthma begins in the first 7 years



J Allergy Clin Immunol 2002; 109:189

Melbourne study: Lung Function Decline according to wheezing frequency



No wheeze

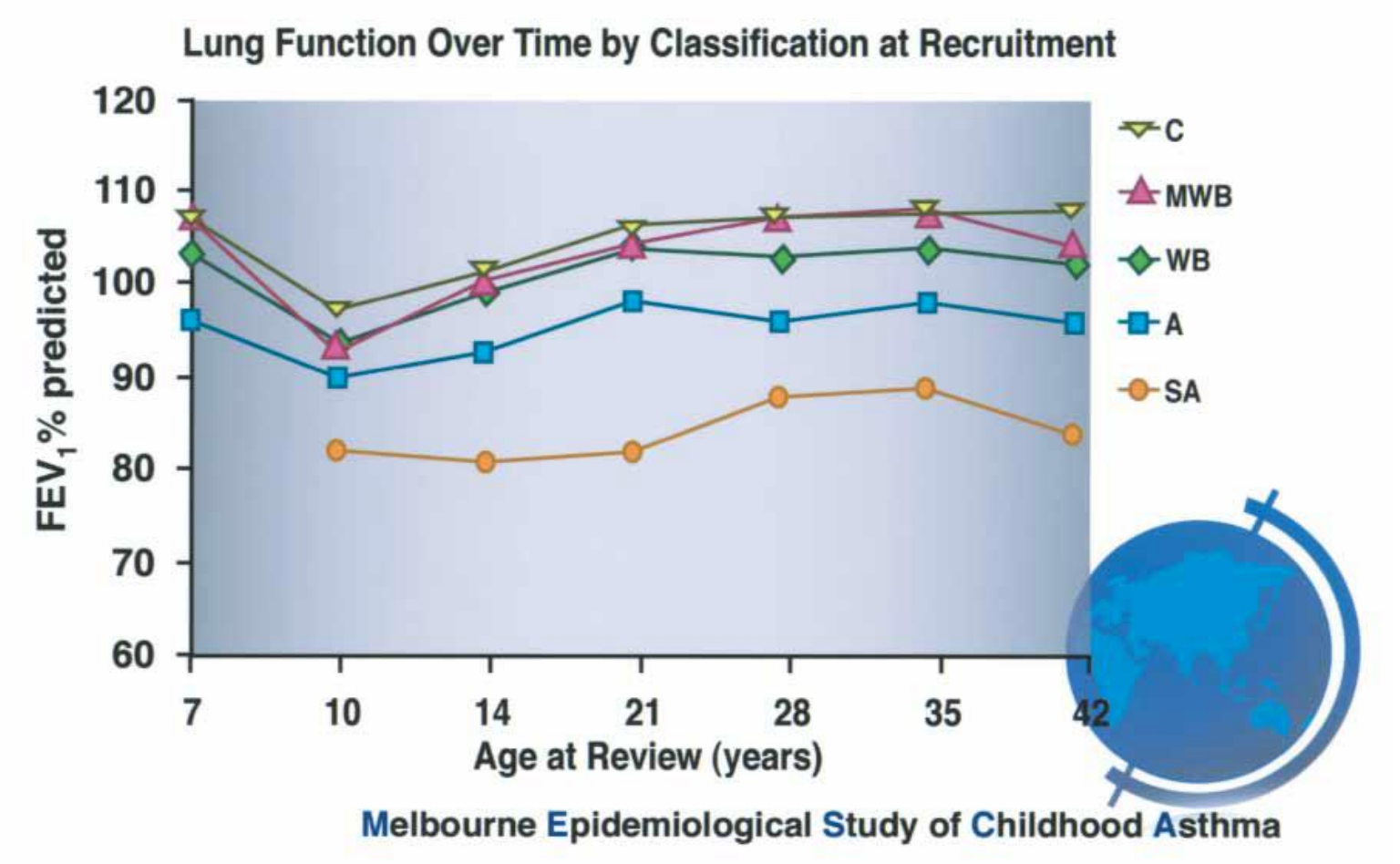
Wheeze, but not in prev. 3mo.

Wheeze < 1/week in prev. 3mo.

Wheezing >1 / week in the previous 3 mo

AM REV RESPIR DIS 1988; 138:26-30

Asthma begins in the first 7 years



J Allergy Clin Immunol 2002; 109:189

Outcomes of childhood asthma to the age of 50 years

Andrew Tai, MBBS, FRACP, PhD,[a] Haily Tran, BBioSc,[b] Mary Roberts, BSc,[c] Nadeene Clarke, BSc,[b] Anne-Marie Gibson, BSc,[b] Suzanna Vidmar, BSc (Hon),[d,e] John Wilson, MBBS, FRACP, PhD,[f] and Colin F. Robertson, MBBS, FRACP, MD[b,c] *North Adelaide, Parkville, Melbourne, and Prahran, Australia*

A group of children with a history of wheezing

Randomly selected after a survey of 30,000 grade 2 Melbourne primary school children in 1963 to 1964 at the age of 7 years

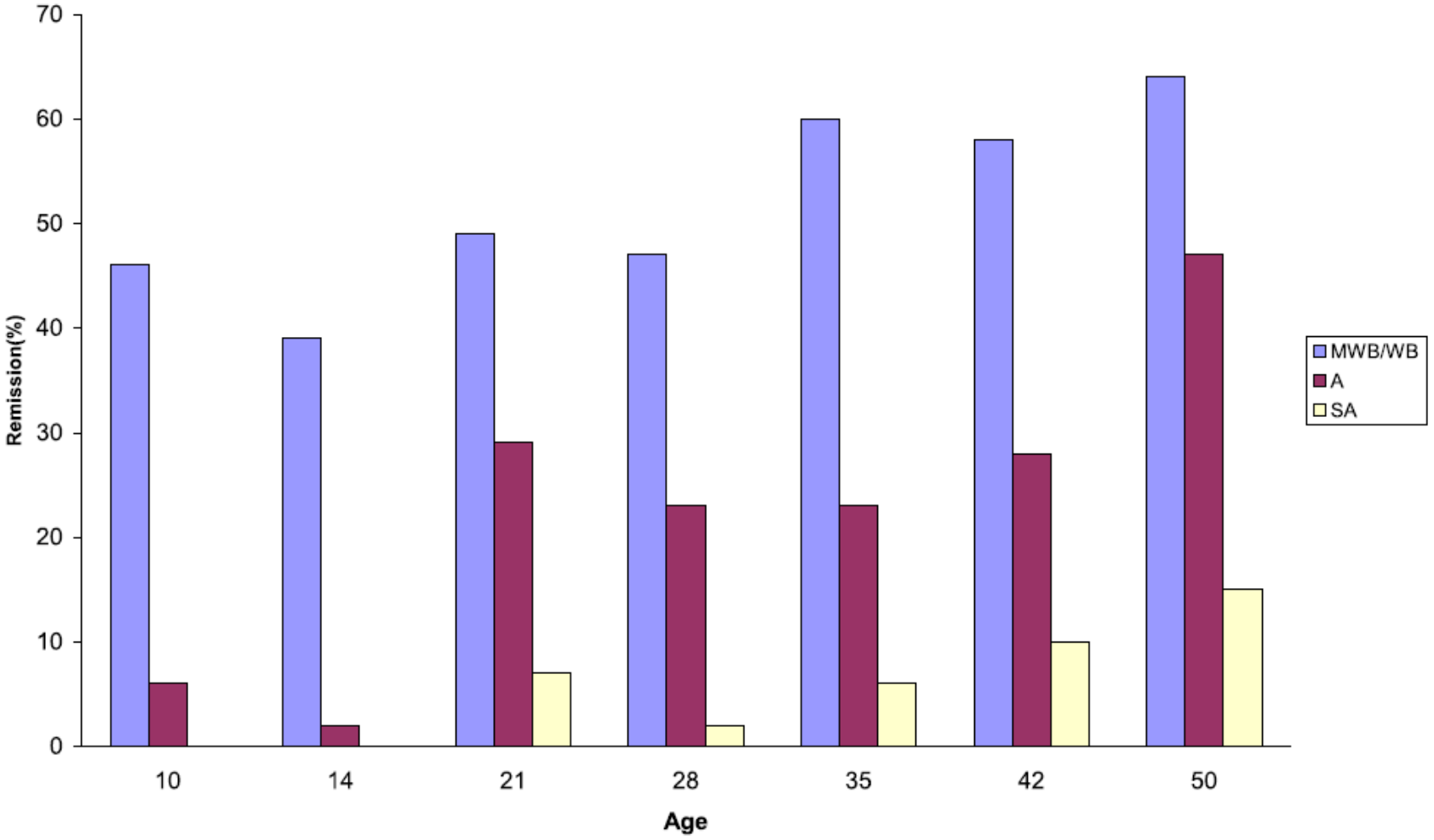
A further group of children with severe wheezing was selected from the same birth cohort at the age of 10 years.

In total, 401 subjects were originally recruited and a further 83 with severe asthma were added to the group.

Reports of wheezing were collected by self report by the parent at recruitment.

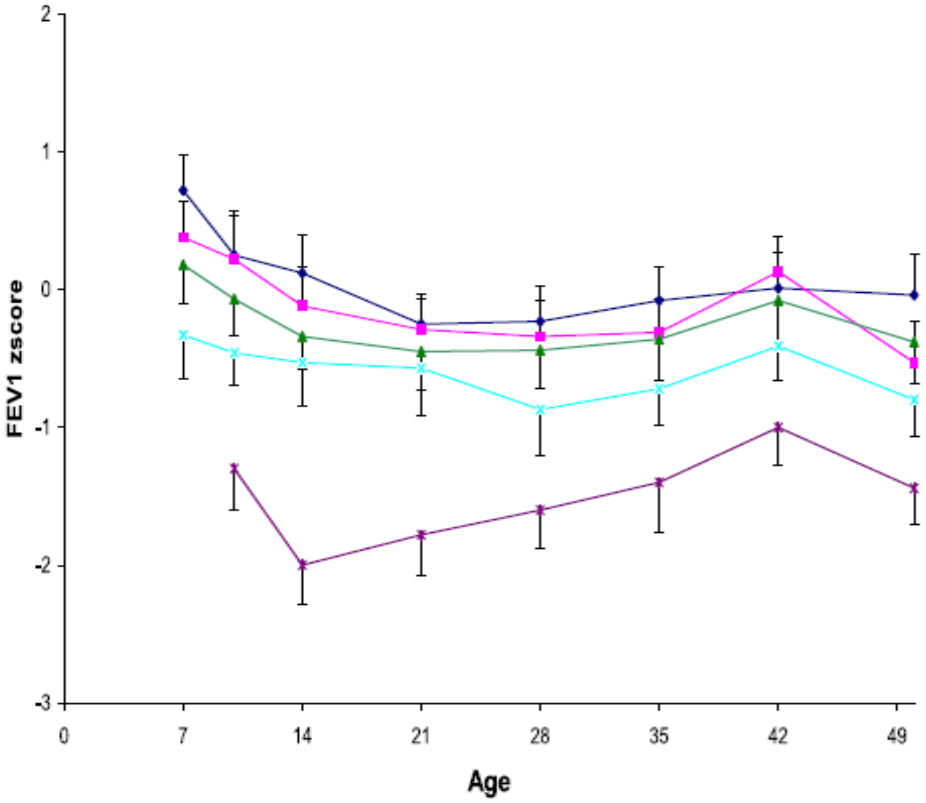
J Allergy Clin Immunol 2014;133:1572-8

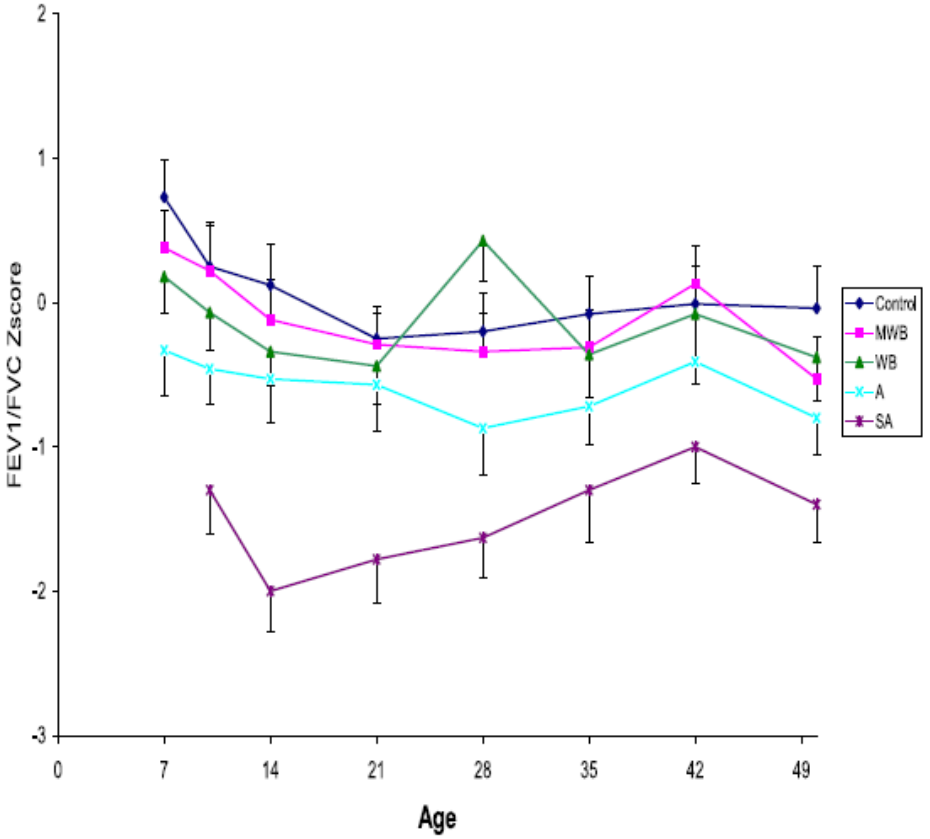
Asthma Remission according to Severity



J Allergy Clin Immunol 2014;133:1572-8

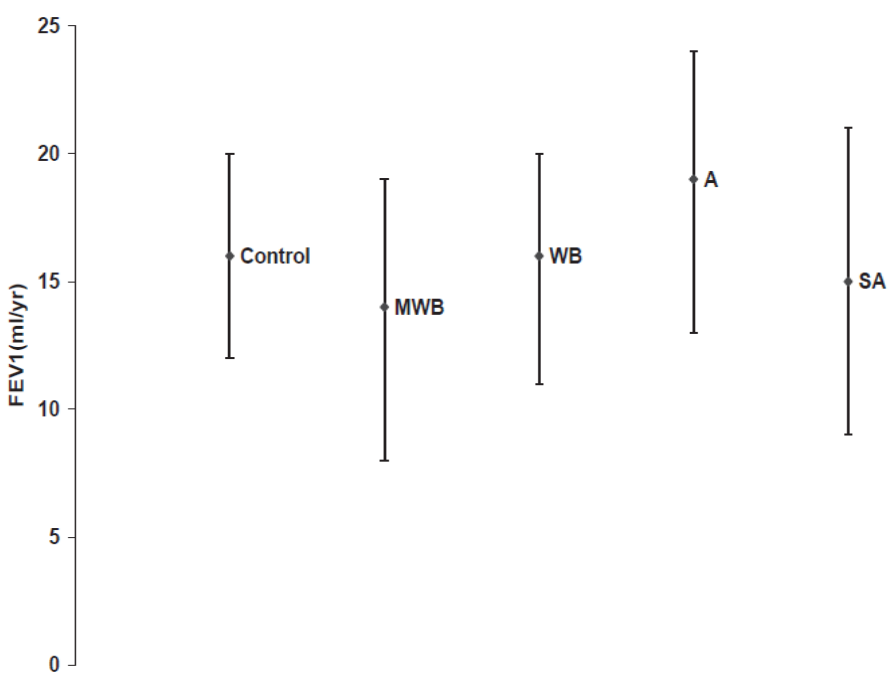
Lung Function by Classification at recruitment

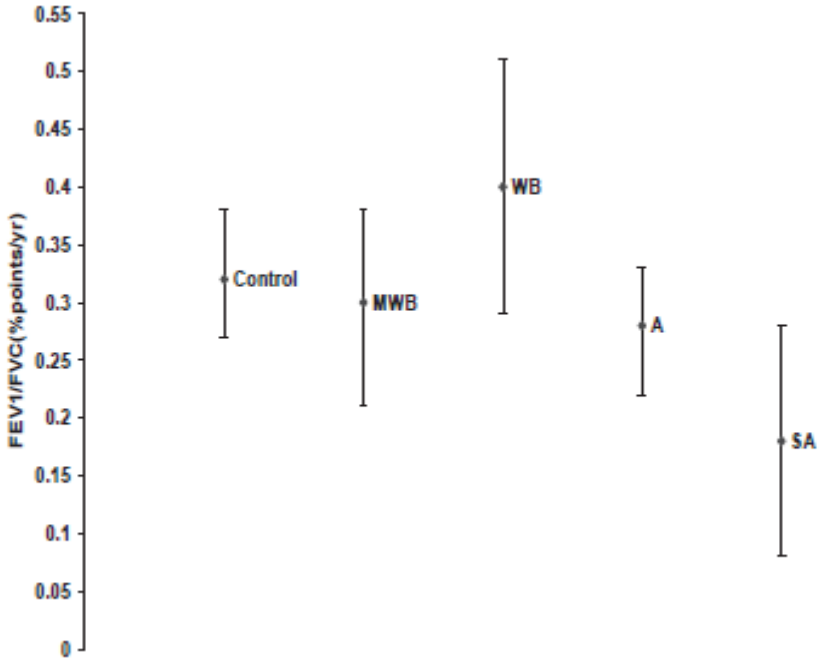




J Allergy Clin Immunol 2014;133:1572-8

Lung Function Decline of age 21~50 years old





J Allergy Clin Immunol 2014;133:1572-8

Mild to moderate asthma affects lung growth in children and adolescents

Robert C. Strunk, MD,[a] Scott T. Weiss, MD,[b] Katherine P. Yates, ScM,[c] James Tonascia, PhD,[c] Robert S. Zeiger, MD, PhD,[d,e] and Stanley J. Szefler, MD,[f] for the CAMP Research Group* *St Louis, Mo, Boston, Mass, Baltimore, Md, La Jolla and San Diego, Calif, and Denver, Colo*

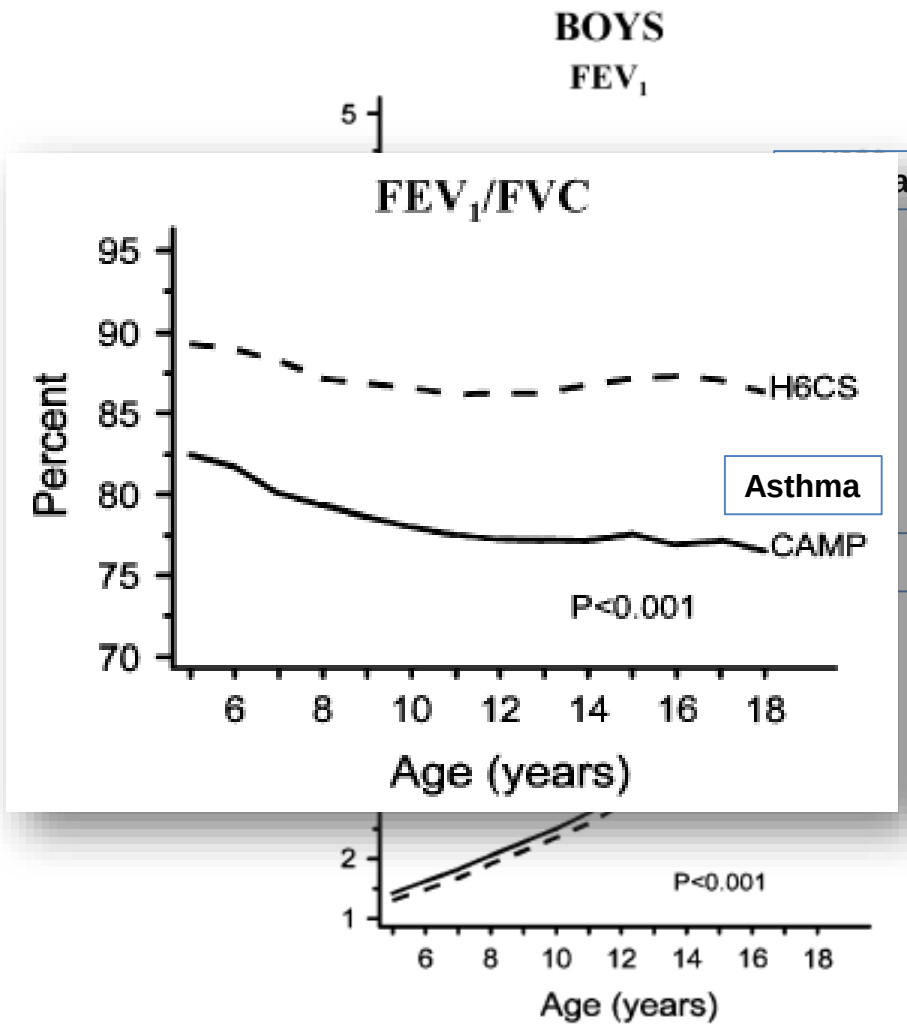
A total of 1041 children with mild to moderate asthma from the Childhood Asthma Management Program (CAMP)

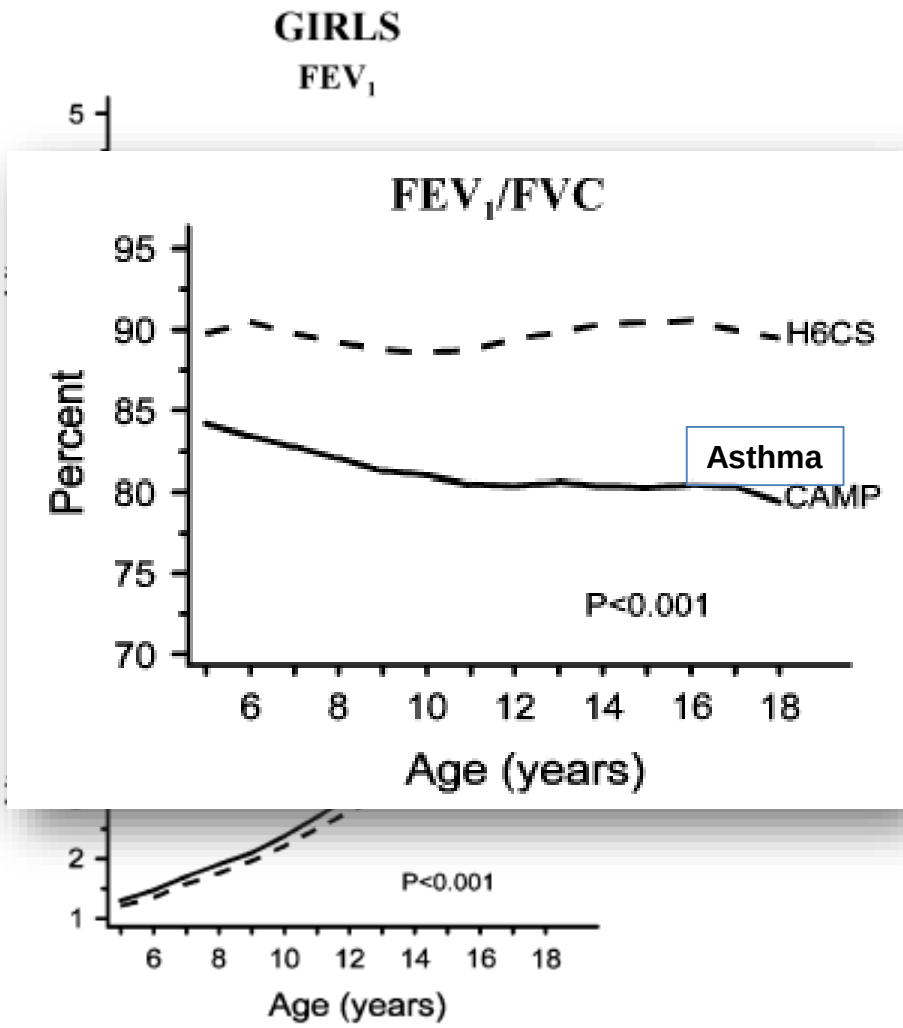
Denver, CO

5415 children without asthma from the Harvard Six Cities Study (H6CS)

J Allergy Clin Immunol 2006;118:1040-7

Lung Function Development in mild to moderate Asthma





J Allergy Clin Immunol 2006;118:1040-7

Participants with $FEV_1/FVC < LLN$

	Boys				Girls			
		Percent abnormal				Percent abnormal		
Age (y)	No. of tests	FEV_1	FVC	FEV_1/FVC	No. of tests	FEV_1	FVC	FEV_1/FVC
5*	127	NA	NA	NA	73	NA	NA	NA
6	391	12.0	2.6	30.7	304	10.8	1.7	33.8
7	625	15.0	3.4	35.4	406	10.1	1.5	31.3
8	867	14.3	3.3	35.2	571	10.0	1.2	32.1
9	1067	12.9	2.0	35.8	708	11.6	3.5	34.2
10	1226	14.3	1.7	37.6	807	12.1	2.9	36.2
11	1295	12.2	1.6	38.2	902	12.4	2.7	36.6
12	1321	14.2	2.0	40.1	921	13.0	1.7	44.3
13	1222	15.4	2.0	40.7	853	12.8	1.9	44.6
14	1115	17.0	2.2	43.1	771	15.8	1.8	46.4
15	967	15.5	2.1	45.5	650	14.2	2.3	46.2
16	753	17.5	2.0	48.2	526	13.5	1.9	47.5
17	577	17.0	1.2	46.1	383	14.1	1.6	46.5
18	415	18.6	0.7	51.6	299	13.0	1.3	50.8
P trend		.047	.085	<.001		.164	.823	<.001

J Allergy Clin Immunol 2006;118:1040-7

Predictors of remitting, periodic, and persistent childhood asthma

Ronina A. Covar, MD,[a] Robert Strunk, MD,[b] Robert S. Zeiger, MD, PhD,[c,d] Laura A. Wilson, ScM,[e] Andrew H. Liu, MD,[a] Scott Weiss, MD, MSc,[f] James Tonascia, PhD,[e] Joseph D. Spahn, MD,[a] and Stanley J. Szefler, MD,[a] for the Childhood Asthma Management Program Research Group *Denver, Colo, St Louis, Mo, San Diego, Calif, Baltimore, Md, and Boston, Mass*

The Childhood Asthma Management Program (CAMP)
1041 children, **5 ~12 years old**, 1993 ~ 1995

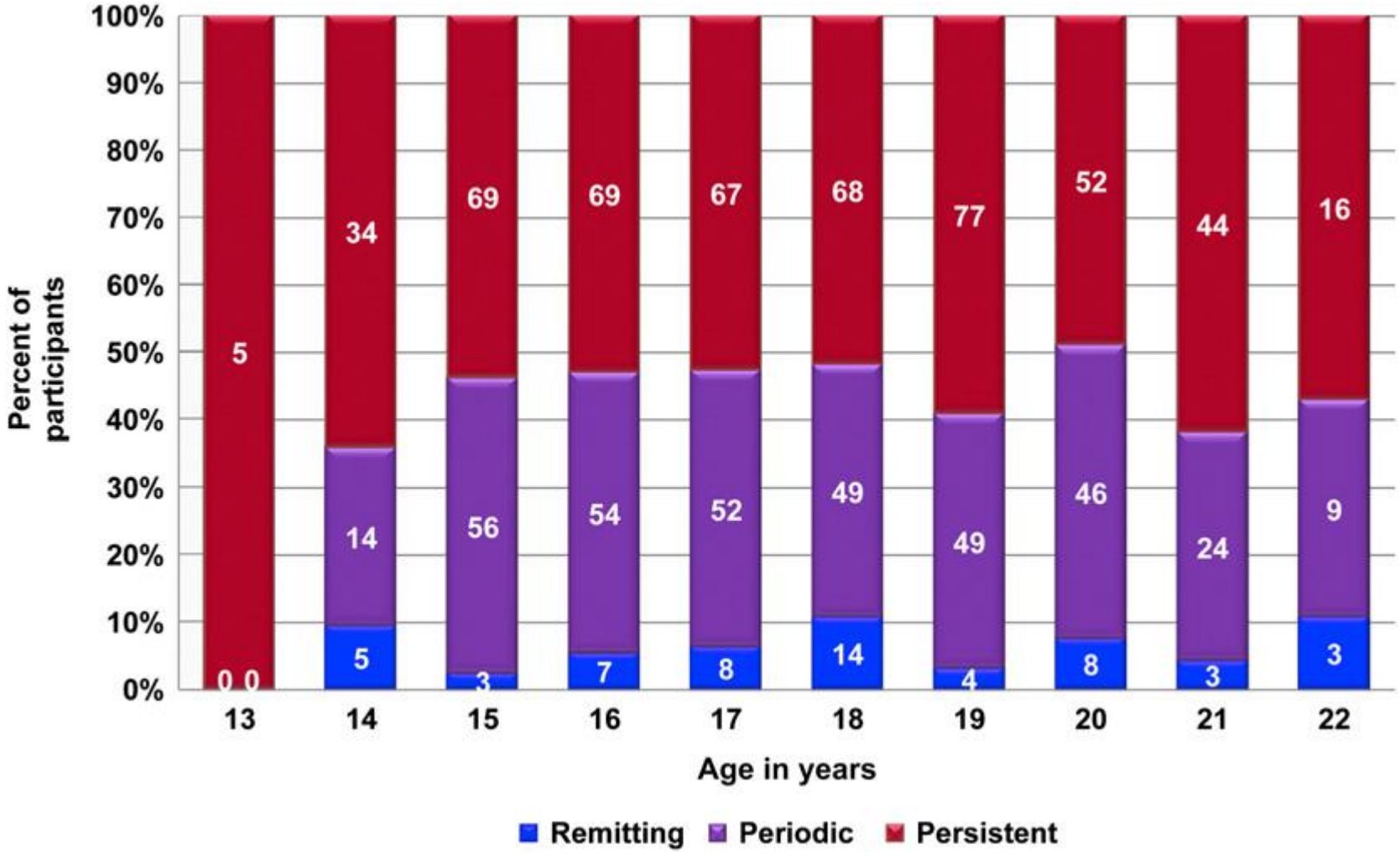
4.3-year randomized, double-masked, multicenter trial in children with mild to moderate persistent asthma

Compared continuous therapy with either budesonide or nedocromil, each to placebo, followed by a 4-year observational follow-up period

Remitting asthma: no asthma activity in the last year
Persistent asthma: asthma activity in every quarter
Periodic asthma: neither remitting nor persistent

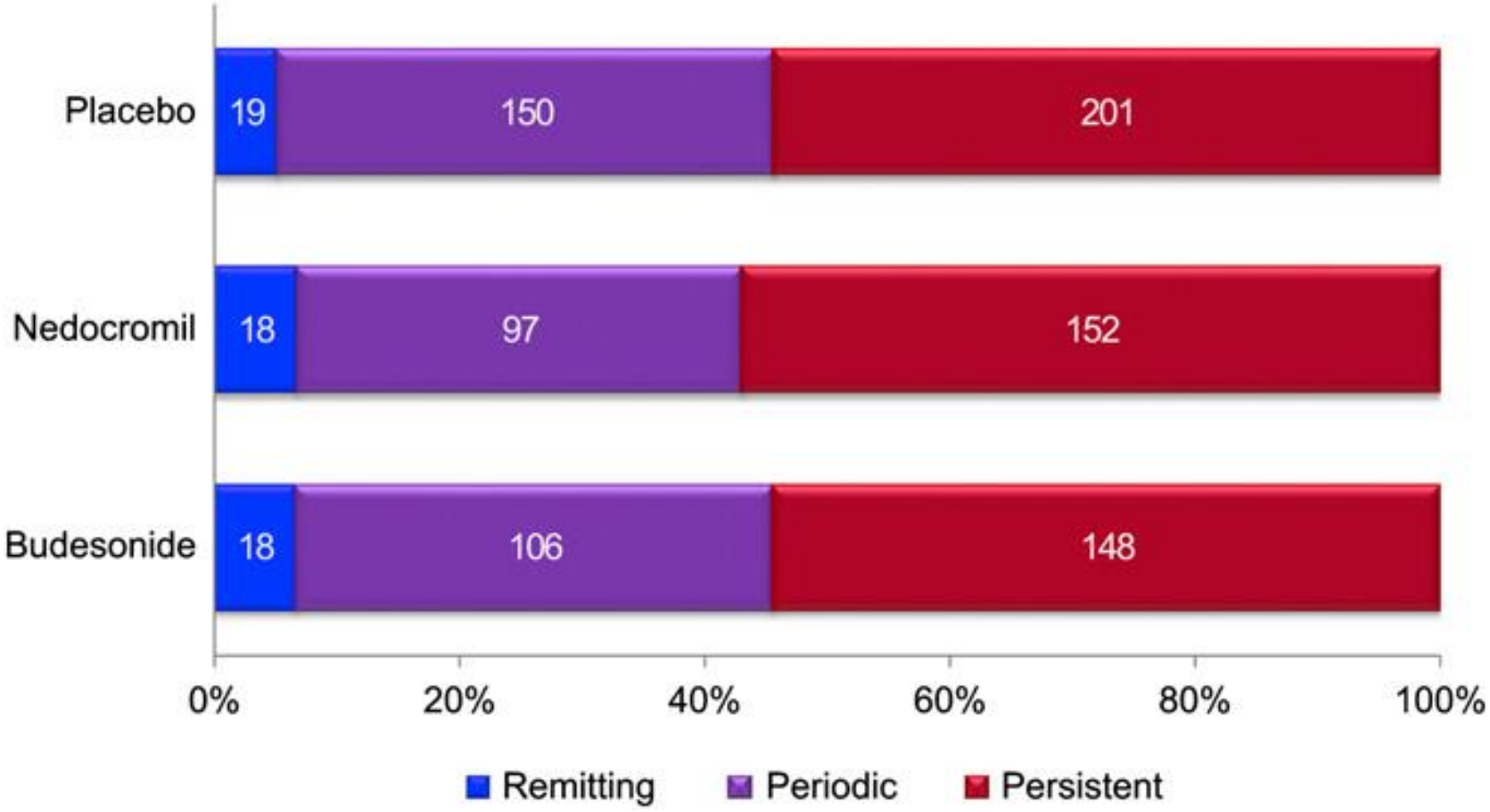
J Allergy Clin Immunol 2010; 125:359

Complete remission is infrequent



J Allergy Clin Immunol 2010; 125:359

No effect noted from earlier anti-inflammatory treatment



J Allergy Clin Immunol 2010; 125:359

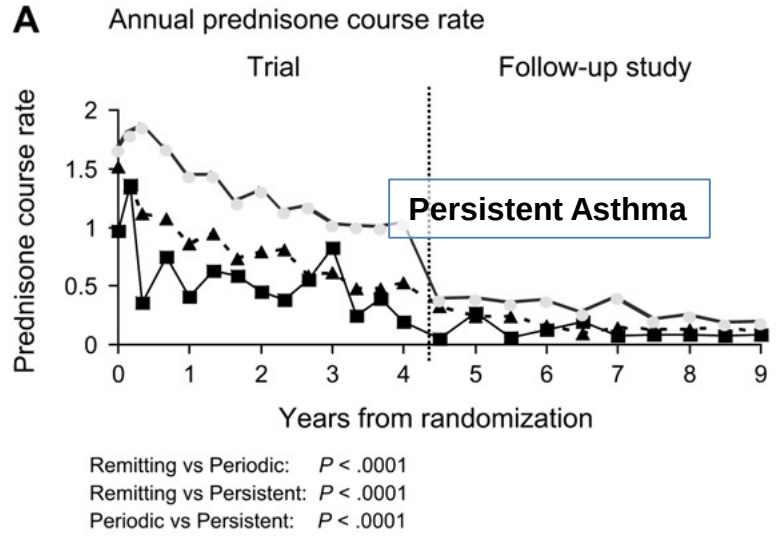
Baseline Characteristics to Progress to Persistent Asthma

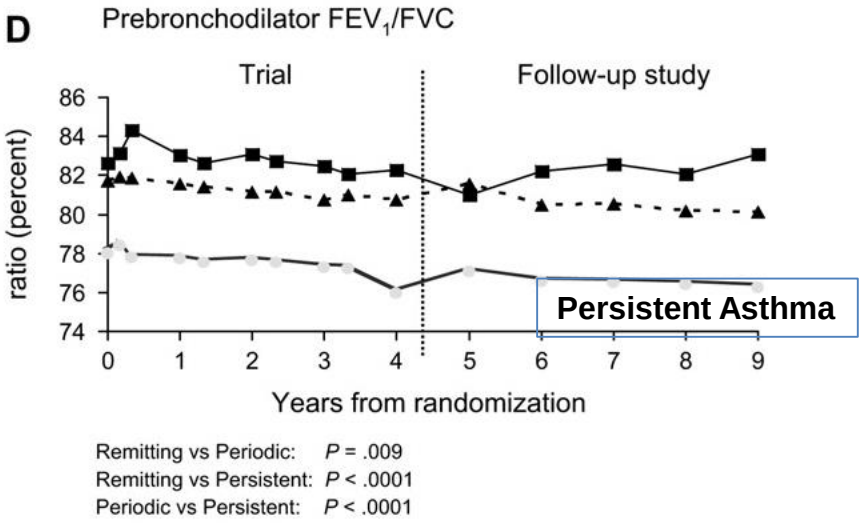
TABLE I. Comparisons of baseline characteristics of the remitting, periodic, and persistent asthma groups

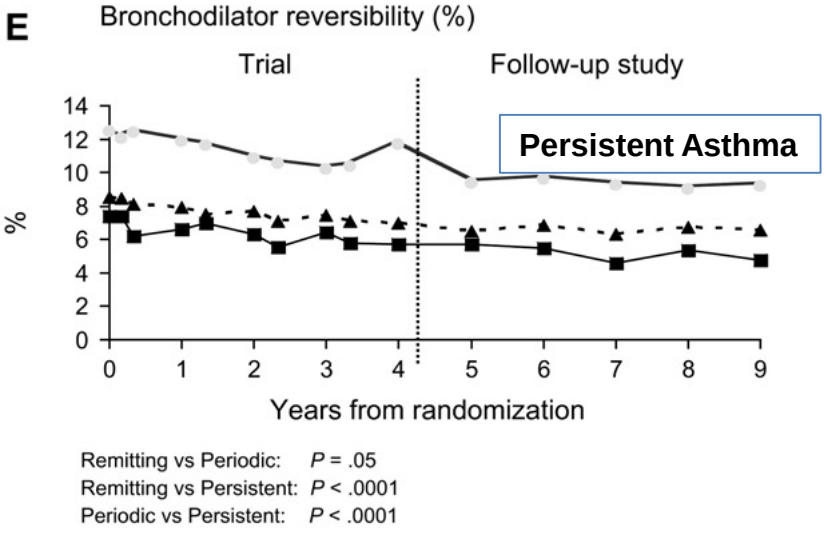
	Periodic (N = 353)	Persistent (N = 501)	*P* value*	*P* value*		
				Remitting vs periodic	Remitting vs persistent	Periodic vs persistent
At least 1 positive skin test (%)	8.9 ± 2.0	8.9 ± 2.2	.84	.68	.59	.76
	61.2	59.9	.91	.93	.78	.70
			.40	.11	.15	.97
No. of positive skin tests	68.3	69.5				
	15.0	14.0				
	9.6	9.2				
	7.1	7.4				
Sensitive and exposed† to indoor allergens (%)	4.5 (2.7-6.4)	5.0 (3.2-6.9)	.12	.50	.84	**.04**
	4.0 (2.0-6.0)	3.0 (2.0-5.0)	.19	.65	.68	.07
	83.0	92.0	**<.0001**	.38	**.001**	**<.0001**
Eczema (%)	4 (1-7)	5 (3-9)	**<.0001**	.78	**.01**	**<.0001**
	64.6	77.1	**<.0001**	**.01**	**<.0001**	**<.0001**
Asth	24.1	31.5	**.02**	.51	.08	**.02**
	51.6	53.7	.82	.87	.89	.53
Asth	15.9	20.6	.21	1.0	.60	.08
	26.3	26.8	.77	.62	.52	.87
Lun		25.3	**.005**	.69	.06	**.004**
			<.001	.17	**.002**	**<.001**
Biomarkers		210 (41.9%)				
		291 (58.1%)				
Serum IgE (ng/mL)		91.3 ± 14.4	**<.0001**	.82	**.03**	**<.0001**
Percent at or above median (433 ng/mL)		102.0 ± 12.9	.11	.41	.84	**.04**
		103.7 ± 13.3	.86	.59	.71	.76
		106.8 ± 12.7	.12	.63	.18	.07
Eosinophil count (cells/μL)		77.9 ± 8.6	**<.0001**	.49	**<.001**	**<.0001**
		84.4 ± 6.7	**<.0001**	.83	**.01**	**<.0001**
		10.4 (5.5-17.5)	**<.0001**	.14	**<.0001**	**<.0001**
		0.8 ± 3.1	**<.0001**	.29	**<.0001**	**<.0001**
Percent at or above median (400 cells/μL)		671 (267-1610)	**<.0001**	.43	**<.001**	**<.0001**
		61.1	**<.0001**	.66	**<.001**	**<.0001**
		471 (261-739)	**<.0001**	.92	**.002**	**<.0001**
		59.8	**<.0001**	.50	**.001**	**<.0001**

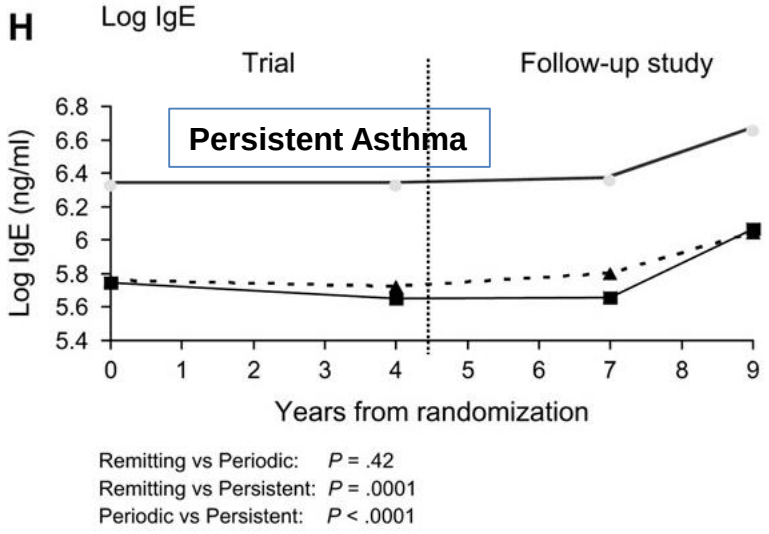
J Allergy Clin Immunol 2010; 125:359

Severe Phenotype in Persistent Asthma









-■- Remitting -▲- Periodic -●- Persistent

J Allergy Clin Immunol 2010; 125:359

Airway Responsiveness in Mild to Moderate Childhood Asthma

Sex Influences on the Natural History

Kelan G. Tantisira[1,2,3], Ryan Colvin[4], James Tonascia[4], Robert C. Strunk[5], Scott T. Weiss[1,3], and Anne L. Fuhlbrigge[1,2], for the Childhood Asthma Management Program Research Group*

[1]Channing Laboratory, [2]Pulmonary Division, and [3]Center for Genomic Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; [4]Childhood Asthma Management Program (CAMP) Coordinating Center, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland; and [5]Department of Pediatrics, Washington University School of Medicine, St. Louis, Missouri

A total of 1,041 children

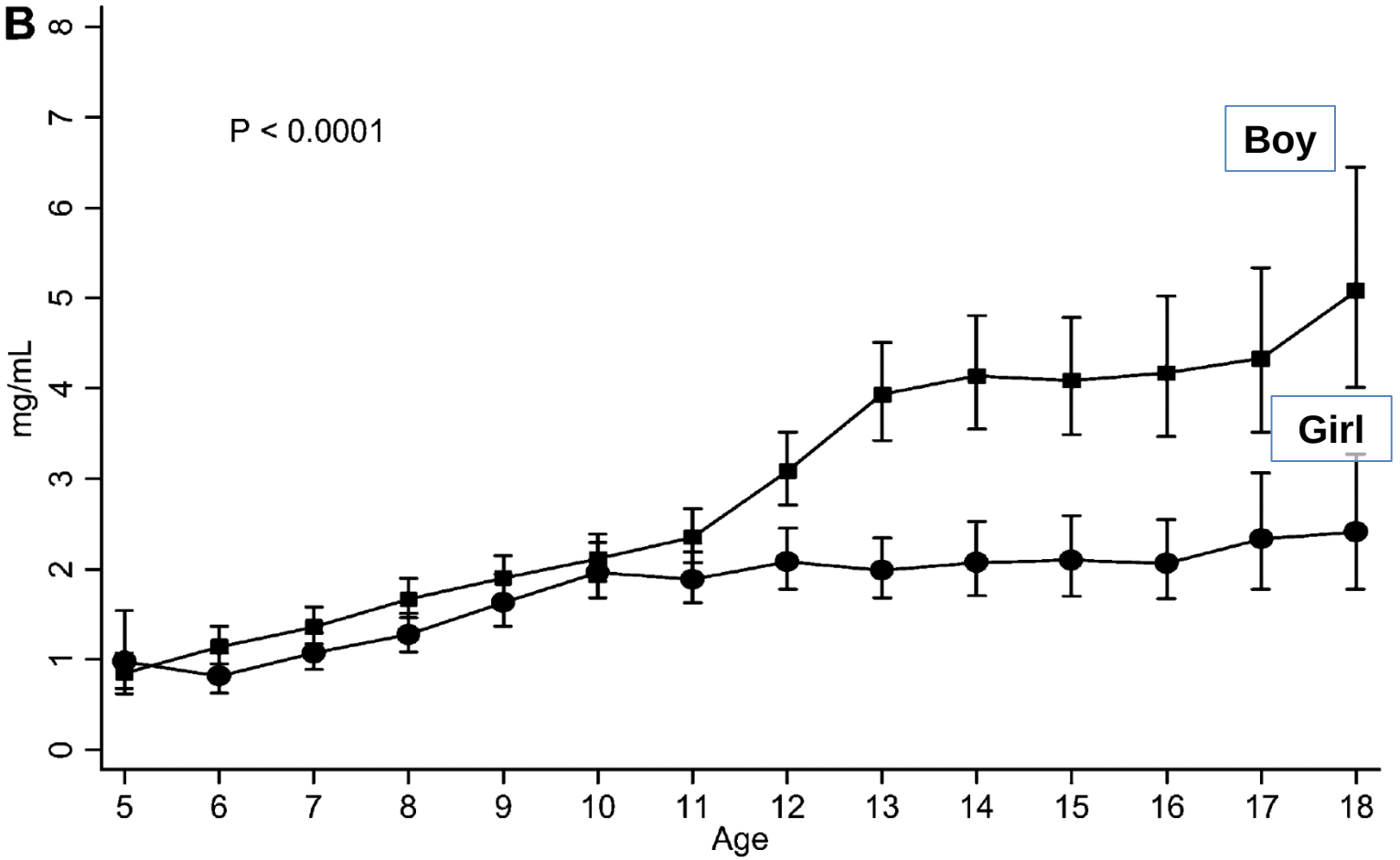
Aged 5–12 years

Mild to moderate persistent asthma

Enrolled in the Childhood Asthma Management Program (CAMP)

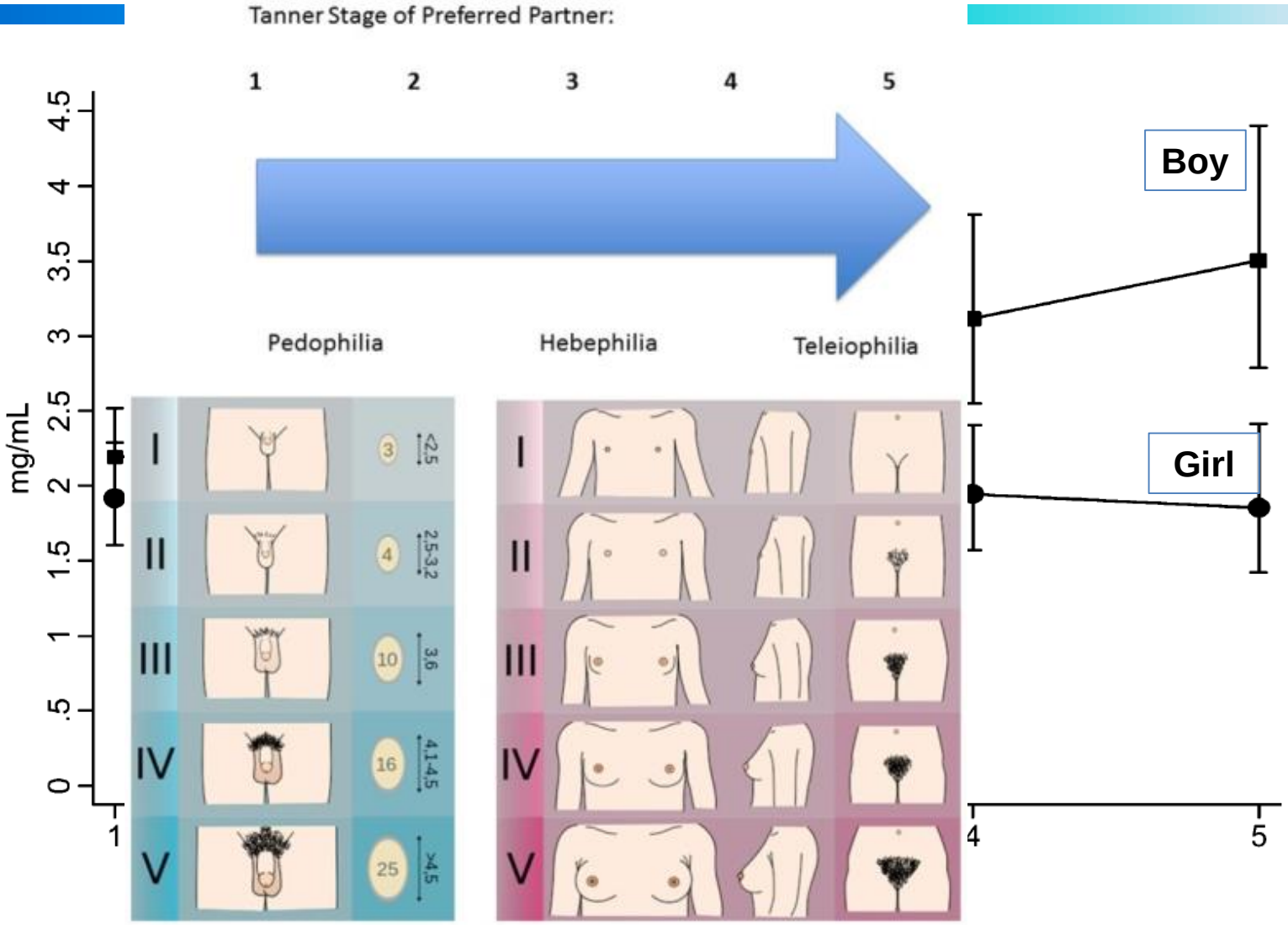
Am J Respir Crit Care Med Vol 178. pp 325–331, 2008

Boys have greater increase after age 11 years than girls



Am J Respir Crit Care Med Vol 178. pp 325–331, 2008

Postpubertal girls had greater airway responsiveness



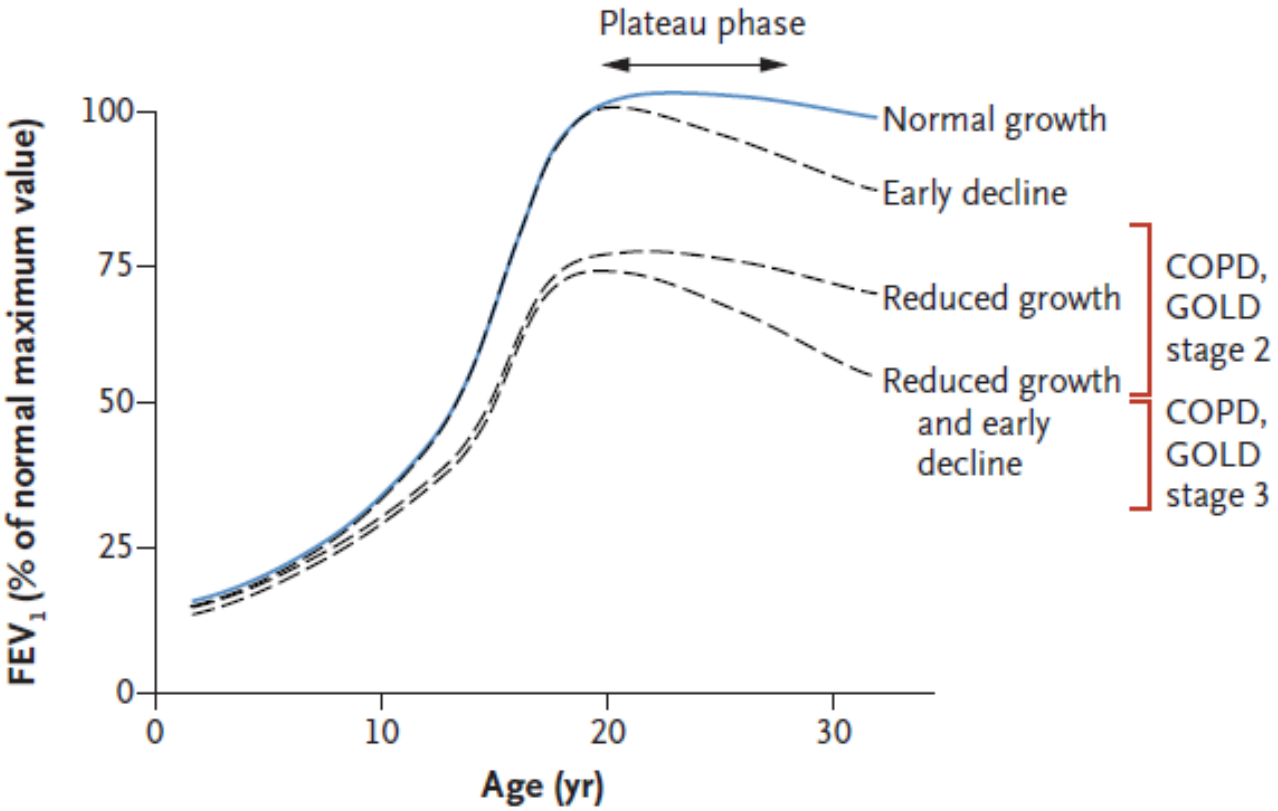
Am J Respir Crit Care Med Vol 178. pp 325–331, 2008

Follow-up study of CAMP: 4 trajectories

ORIGINAL ARTICLE

Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma

M.J. McGeachie, K.P. Yates, X. Zhou, F. Guo, A.L. Sternberg, M.L. Van Natta, R.A. Wise, S.J. Szefler, S. Sharma, A.T. Kho, M.H. Cho, D.C
P.J. Castaldi, G. Jain, A. Sanyal, Y. Zhan, B.R. Lajoie
J. Stamatoyannopoulos, R.A. Covar, R.S. Zeiger, N.F. Adkin
H.W. Kelly, H. Grasemann, J.M. Vonk, G.H. Koppelman, D.S
I. Houston, Q. Lu, A.L. Fuhlbrigge, K.G. Tantisira, E.K. Silve
S.T. Weiss, and R.C. Strunk, for the CAMP Researc



N Engl J Med 2016;374:1842-52

Follow-up study of CAMP: 4 trajectories

Characteristic	Normal Growth (N=170)	Normal Growth and Early Decline (N=178)	Reduced Growth (N=160)	Reduced Growth and Early Decline (N=176)	P Value†
Maximum lung function attained — no. (%)	45 (26)	178 (100)	30 (19)	176 (100)	<0.001
Age at maximum lung function — yr	22.3±2.2	20.6±2.2	21.9±1.7	20.6±1.8	<0.001
Plateau phase					<0.001
Plateau not attained, maximum lung function not reached — no. (%)	125 (74)	0	130 (81)	0	
No plateau, immediate decline — no. (%)	0	112 (63)	0	106 (60)	
Maximum lung function reached, plateau attained — no. (%)	45 (26)	66 (37)	30 (19)	70 (40)	
ed — yr	22.3±2.2	20.6±2.1	21.9±1.7	20.5±1.6	<0.001
d — no. (%)	1 (1)‡	66 (37)	—	70 (40)	0.60
r	2.0‡	1.5±0.6	—	1.8±0.9	0.03
)	1 (1)‡	178 (100)	0	176 (100)	
Had an early decline — no. (%)	0	178 (100)	0	176 (100)	
Age at start of any decline — yr	24.0‡	21.1±2.3	—	21.3±2.0	0.46
Demographic and physical characteristics					
		(56)	114 (71)	109 (62)	<0.001
		±1.7	9.3±1.8	9.9±1.7	0.006
		(60)	112 (70)	106 (60)	0.04
Body-mass index at randomization — z score	0.50±0.97	0.78±0.94	0.18±1.04	0.44±1.05	<0.001
Interval between diagnosis of asthma and enrollment — no. (%)					0.003
<3 yr	50 (29)	45 (25)	31 (19)	28 (16)	
3–6 yr	85 (50)	84 (47)	81 (51)	79 (45)	
≥7 yr	35 (21)	49 (28)	48 (30)	69 (39)	
Maternal cigarette smoking during gestation — no. (%)	17 (10)	27 (15)	20 (12)	27 (15)	0.40
Lung function at randomization					
Prebronchodilator FEV_1 — % of predicted value	100.5±13.4	99.7±12.9	87.5±12.6	83.8±12.9	<0.001
Prebronchodilator FEV_1:FVC — % of predicted value	81.9±6.9	81.6±7.5	76.5±7.9	76.5±8.4	<0.001
Bronchodilator response — %¶	8.9±7.8	8.2±7.8	12.7±9.9	12.4±11.3	<0.001
Airway responsiveness — log mg/ml‖	0.3±1.2	0.4±1.1	−0.2±1.1	−0.2±1.1	<0.001
Lifetime smoking — pack-yr**	0.5±1.5	0.4±1.4	0.4±1.1	0.5±1.5	0.97
Age and spirometry at last visit					
Age — yr	25.7±1.7	26.0±1.8	25.8±1.9	26.3±1.7	0.01
Prebronchodilator FEV_1 — % of predicted value	104.3±7.6	97.7±9.5	87.1±7.9	79.7±10.0	<0.001
Prebronchodilator FEV_1:FVC — % of predicted value	80.4±6.4	78.1±7.2	73.0±8.0	71.2±9.6	<0.001

Male sex — no. (%)

Lung function at randomization

N Engl J Med 2016;374:1842-52

A 15-YEAR FOLLOW-UP STUDY OF VENTILATORY FUNCTION IN ADULTS WITH ASTHMA

PETER LANGE, M.D., PH.D., JAN PARNER, JØRGEN VESTBO, M.D., PH.D., PETER SCHNOHR, M.D., AND GORM JENSEN, M.D., PH.D.

A longitudinal epidemiologic study of the general population
Danish, Copenhagen

Adults with self-reported asthma and adults without asthma.

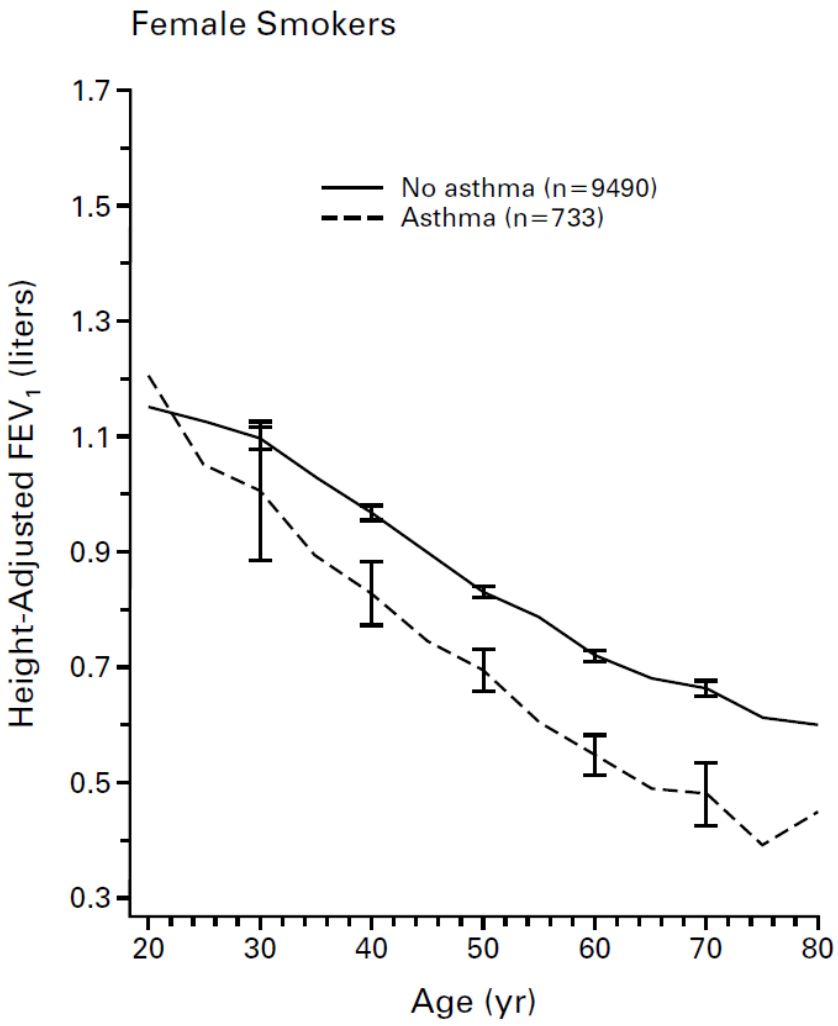
The study was conducted between 1976 and 1994

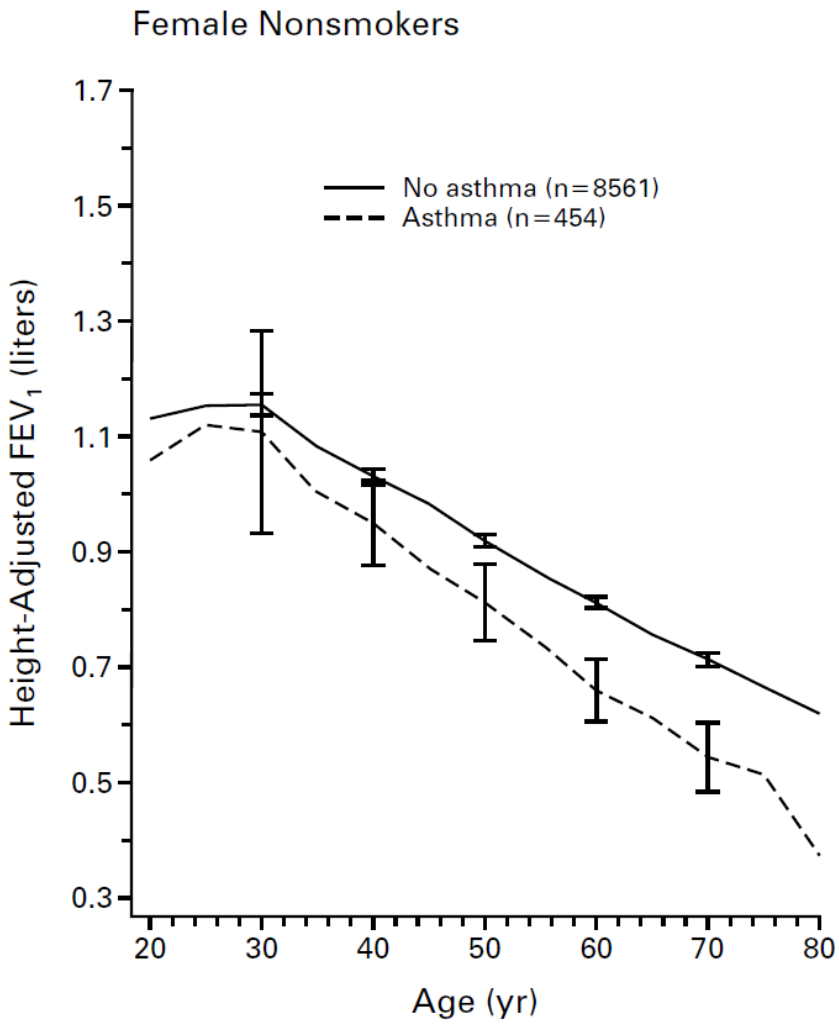
Three measurements of lung function were obtained over a 15-year period.

The final data set consisted of measurements from 17,506 subjects (8136 men and 9370 women), of whom 1095 had asthma.

Am J Respir Crit Care Med Vol 178. pp 325–331, 2008

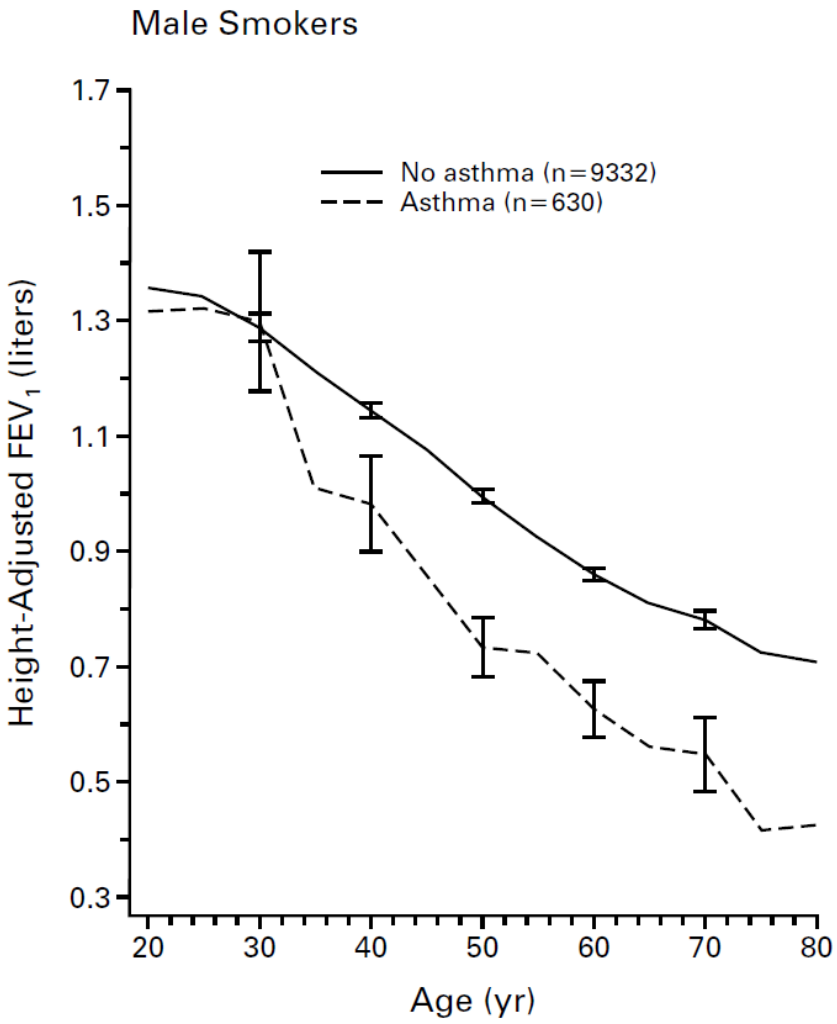
Substantially greater declines in Asthma

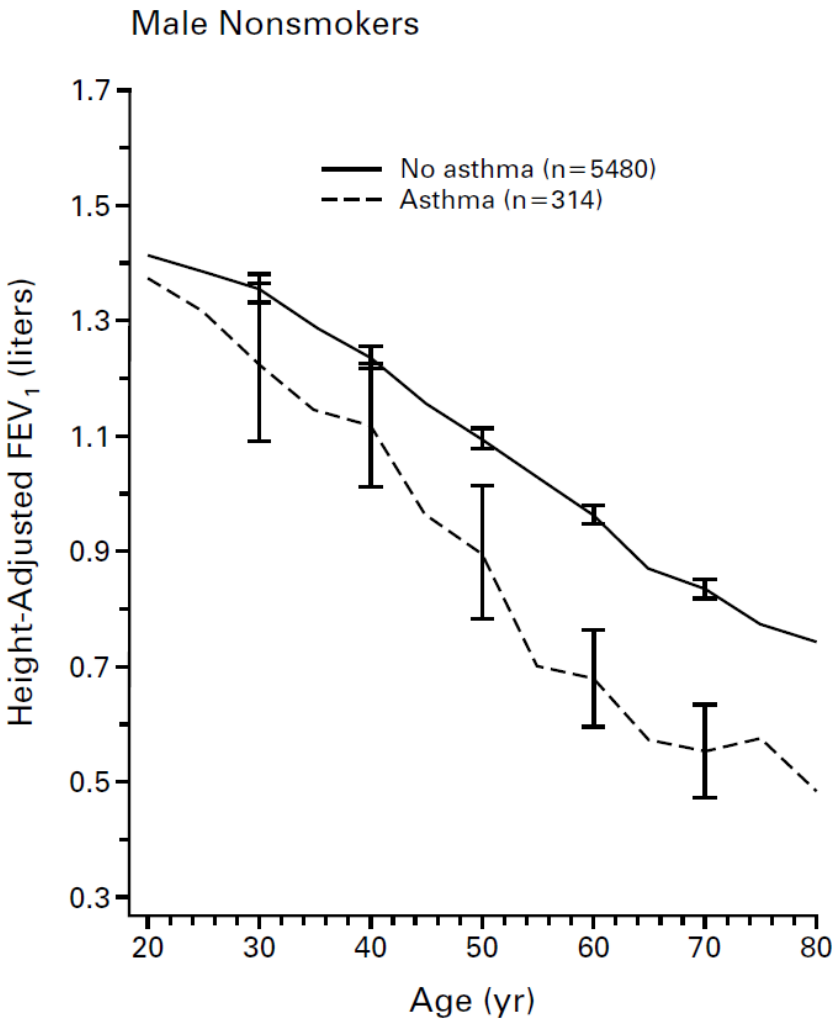




N Engl J Med 1998;339:1194-200

Substantially greater declines in Asthma





N Engl J Med 1998;339:1194-200

Summary

- Asthma phenotype was decided around 6 years old.
- Severity, Parental Asthma History and Allergic Phenotype (IgE, Skin test, Eczema) predict persistent asthma.
- Lung function cannot come into full bloom, if persists.
- No definite therapy to remit asthma.