6° Corso
Novità in Allergologia ed Immunologia Pediatrica
Benevento 18 – 19 Maggio 2012

LA COPD inizia in età pediatrica?

Bambino Gesù
OSPEDALE PEDIATRICO

Renato Cutrera
Dir. U.O.C. Broncopneumologia
Dipartimento Medicina Pediatrica (Prof. A.G. Ugazio)
Ospedale Pediatrico Bambino Gesù IRCCS


64 million people COPD worldwide in 2004 (WHO)

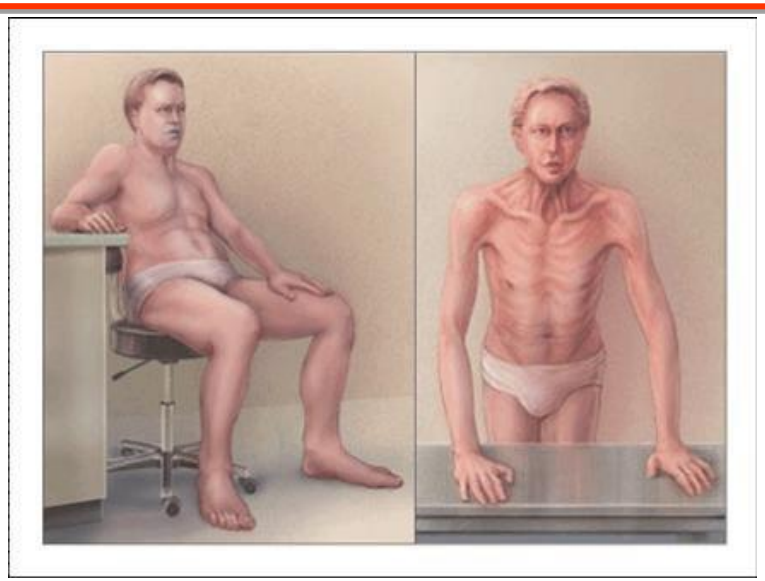
The primary cause of COPD is tobacco smoke (through tobacco use or second-hand smoke).

Definition of COPD

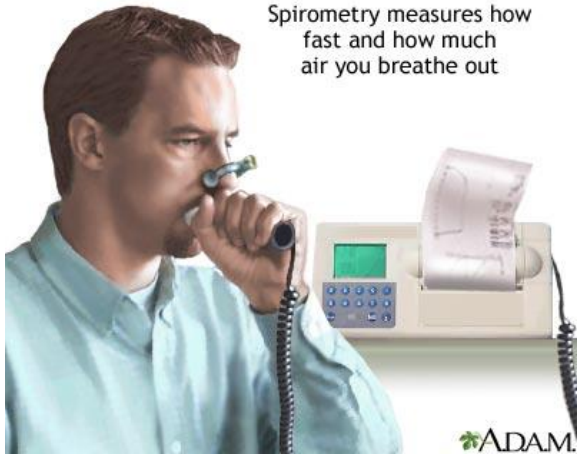
- COPD, a common preventable and treatable disease, is characterized by **persistent airflow limitation** that is usually **progressive** and associated with an enhanced **chronic inflammatory** response in the airways and the lung to noxious particles or gases.
- **Exacerbations and comorbidities** contribute to the overall severity in individual patients.

Diagnosis and Assessment: Key Points

- A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.

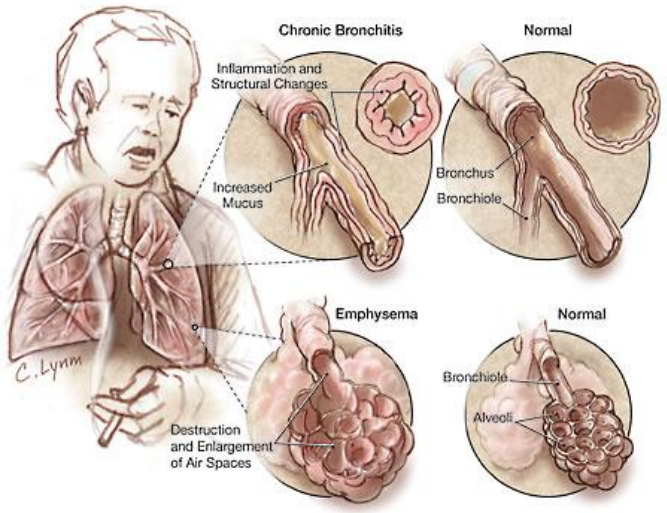


- Spirometry is *required* to make the diagnosis; the presence of a post-bronchodilator $FEV_1/FVC < 0.70$



Small Airways Disease

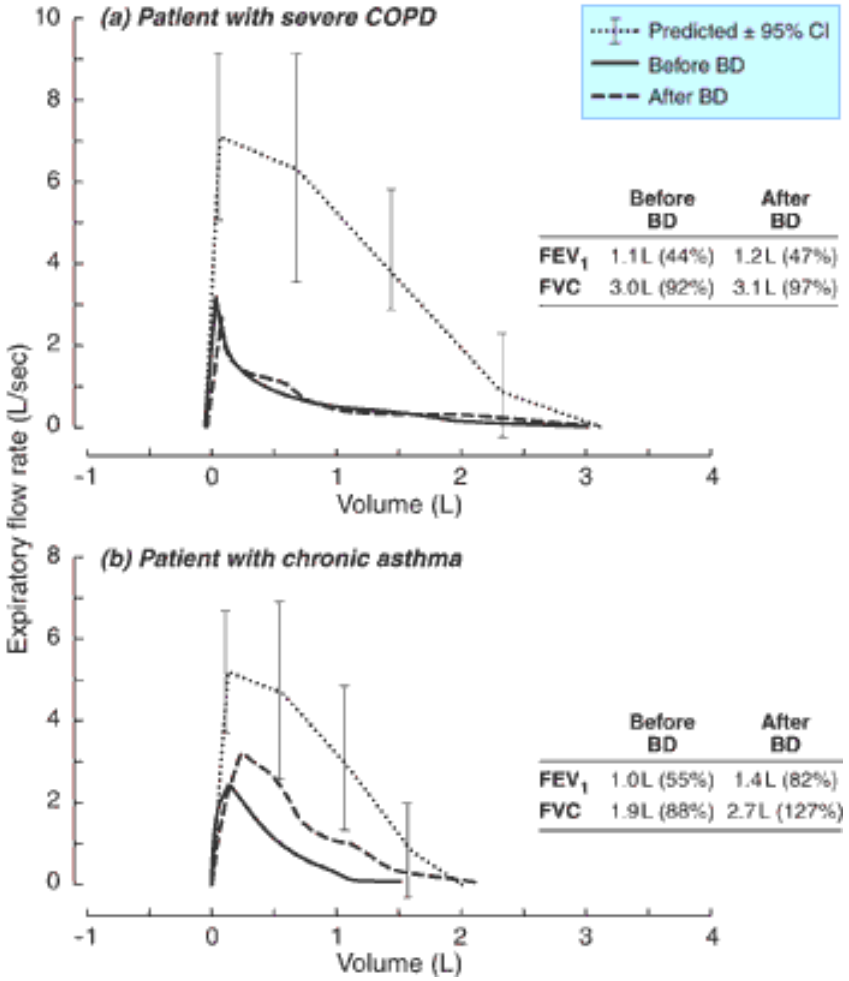
- Airway inflammation
- Airway fibrosis, luminal plugs
- Increased airway resistance



Parenchymal Destruction

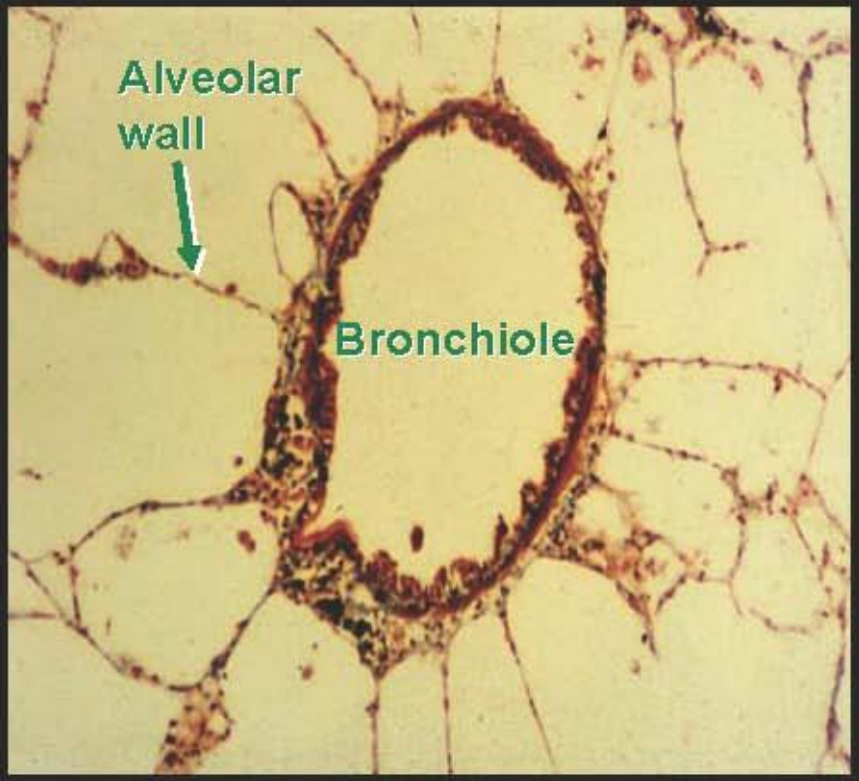
- Loss of alveolar attachments
- Decrease of elastic recoil

AIRFLOW LIMITATION

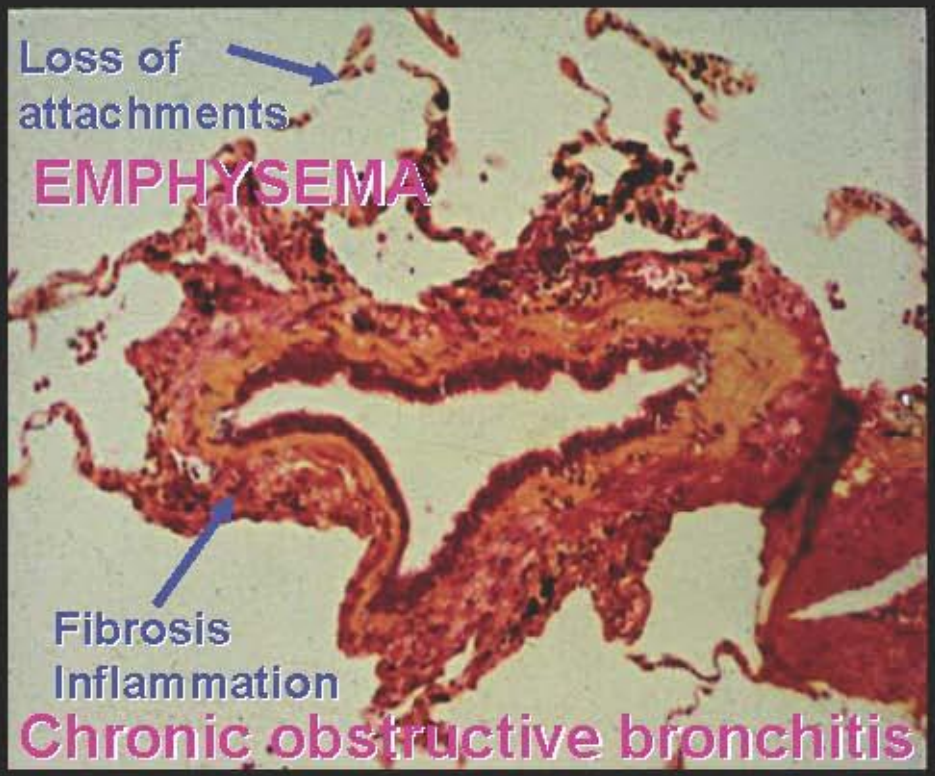


PATHOLOGY OF COPD

Peripheral lung



Normal



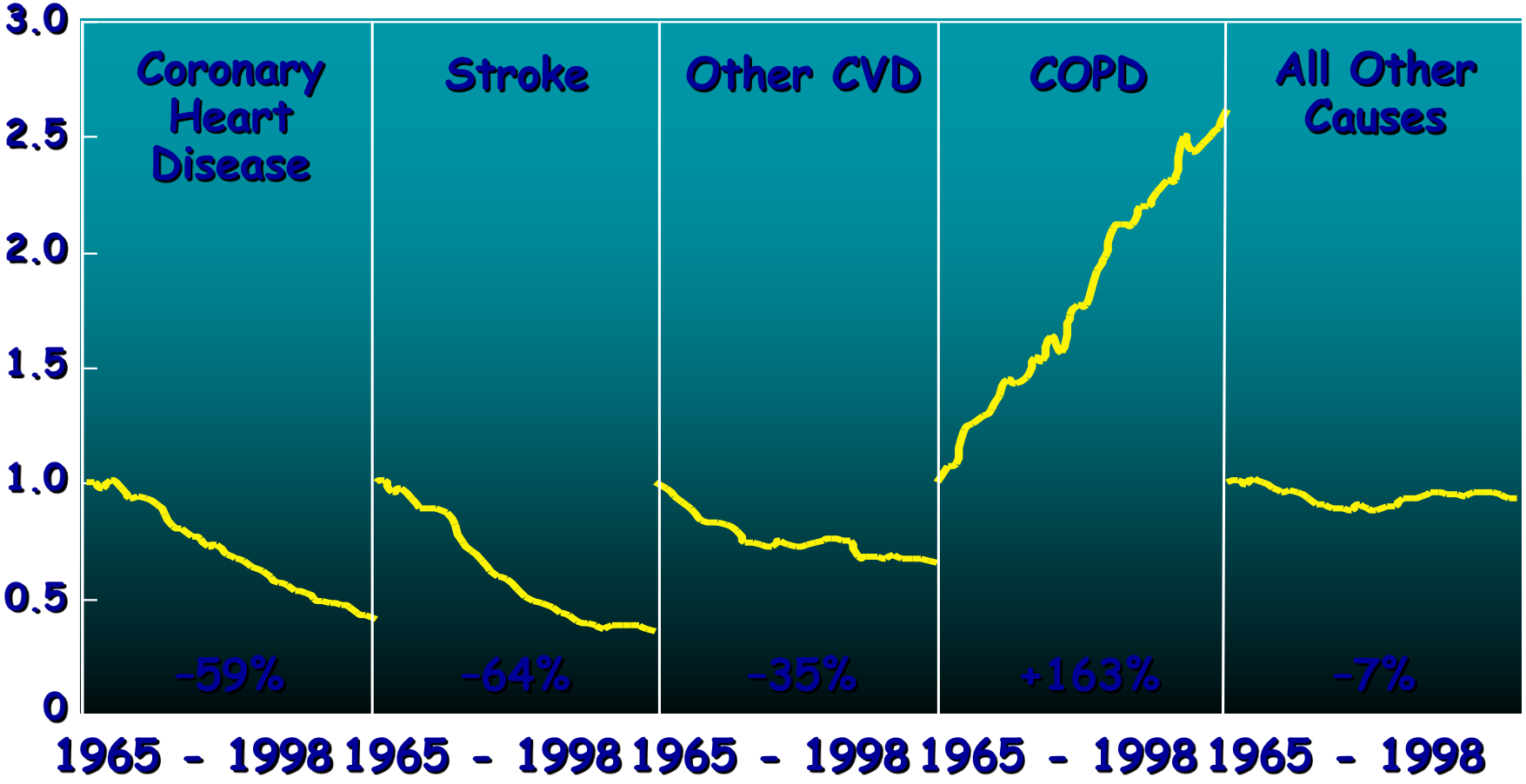
COPD

Dr Manuel Cosio

Burden of COPD

- COPD is a leading cause of morbidity and mortality worldwide.
- The burden of COPD is projected to increase in coming decades due to continued exposure to COPD risk factors and the aging of the world's population.
- COPD is associated with significant economic burden.

Proportion of 1965 Rate (USA)



More than 3 million people died of COPD in 2005, which is equal to 5% of all deaths globally that year

Risk Factors for COPD

Genes

Exposure to particles

- **Tobacco smoke**
- Occupational dusts, organic and inorganic
- **Indoor air pollution** from heating and cooking with biomass in poorly ventilated dwellings
- **Outdoor air pollution**

Lung growth and development

Gender

Age

Respiratory infections

Socioeconomic status

Asthma/Bronchial hyperreactivity

Chronic Bronchitis

COPD - FATTORI DI RISCHIO

Fattori ambientali

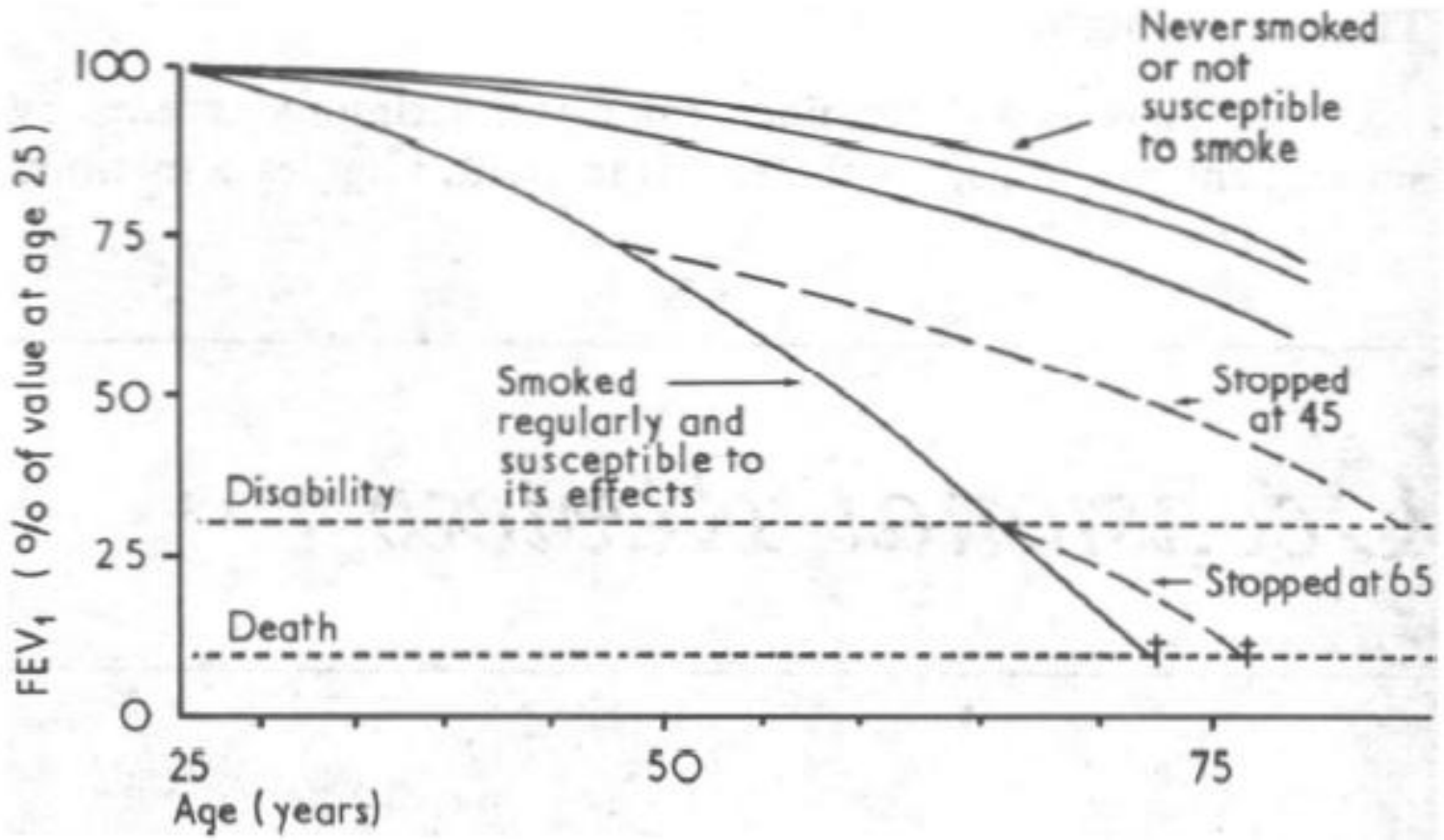
- Fumo di sigaretta
- Fumo passivo
- Fumo materno
- Inquinamento outdoor, indoor
- Esposizione professionale
- Crescita del polmone
- Nutrizione
- Infezioni respiratorie

Fattori individuali

- Deficit alfa1-AT
- Stress ossidativo
- Basso peso alla nascita
- Funzione respiratoria nei primi mesi di vita

Model of changes of lung function in healthy subjects

Fletcher & Peto BMJ 1977



Model of changes of lung function in healthy subjects

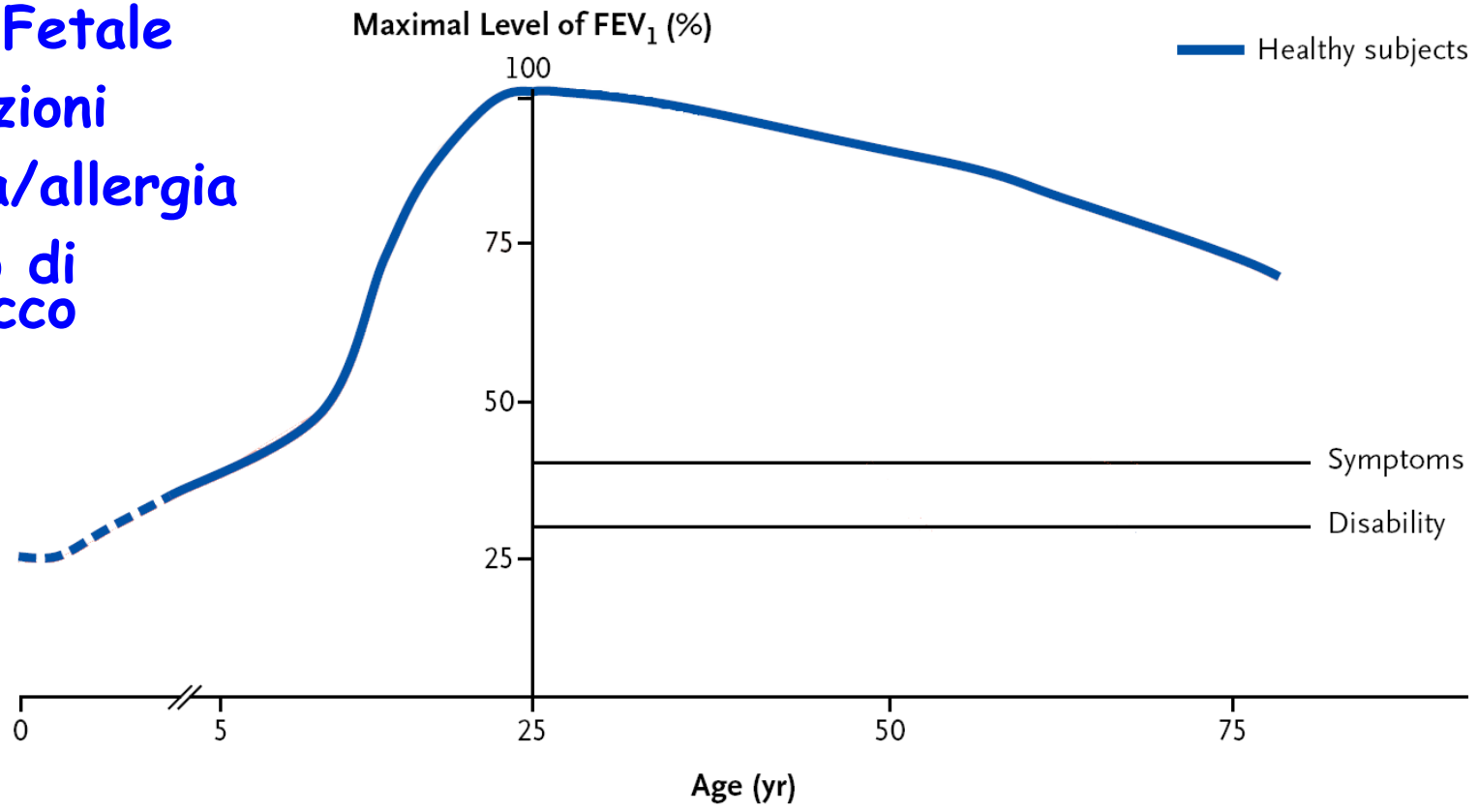
Fletcher & Peto BMJ 1977

Vita Fetale

Infezioni

Asma/allergia

Fumo di tabacco



Chronic diseases associated with the fetal origins of adult disease (FOAD) hypothesis

Chronic diseases attributed to "developmental origins"

- Diabetes mellitus
- Obesity
- Dyslipidemia
- Hypertension
- Coronary artery disease
- Stroke
- Kidney failure—glomerulosclerosis
- Liver failure—cholestasis, steatosis
- Lung abnormalities—BPD, reactive airway disease
- Immune dysfunction
- Reduced bone mass
- Alzheimer's disease
- Depression, anxiety, bipolar disorder, schizophrenia
- Cancer

PubMed Central
Search | Journal List
BMJ helping doctors make better decisions
Search | Latest content
ournal List > BMJ > v.303(6804); Sep 21, 1991
BMJ. 1991 September 21; 303(6804): 671–675. PMCID: PMC1670943

Relation of birth weight and childhood respiratory infection to adult lung function and death from chronic obstructive airways disease.

D J Barker, K M Godfrey, C Fall, C Osmond, P D Winter, and S O Shaheen

Hertfordshire, England.

SUBJECTS:

5718 men born in the county during 1911-30 and a subgroup of 825 men born in the county during 1920-30 and still living there.

MAIN OUTCOME MEASURES:

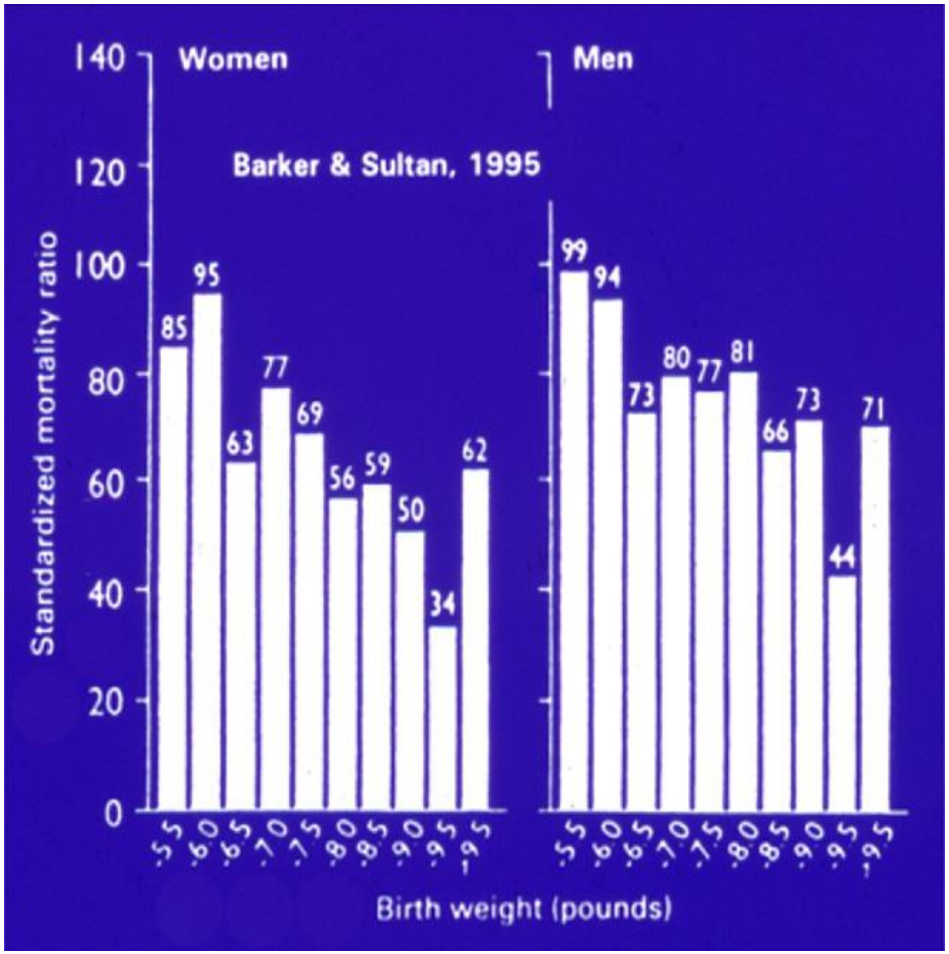
Death from chronic obstructive airways disease, mean forced expiratory volume in one second (FEV1) and forced vital capacity (FVC), and respiratory symptoms.

TABLE II—*Mean forced expiratory volume in one second adjusted for height and age among men aged 59-70, according to birth weight*

Birth weight (lb)	No of men	Forced expiratory volume (l)
≤5·5	33	2·28
−6·5	103	2·41
−7·5	258	2·44
−8·5	242	2·52
−9·5	132	2·55
>9·5	57	2·57
All	825	2·48*

*Standard deviation=0·59.

the "Barker hypothesis," or "fetal origins of adult disease"



Standardized mortality ratio by gender based on birth weight in pounds (1 pound= 0.45 Kg)

Calkins K, Curr Probl Pediatr Adolesc Health Care 2011;41 158-176

TABLE III—*Mean forced expiratory volume in one second (litres) adjusted for height and age among men aged 59-67, according to birth weight and bronchitis or pneumonia and whooping cough in infancy. Numbers of men in parentheses*

Birth weight (lb)	Bronchitis or pneumonia in infancy		Whooping cough in infancy	
	Absent	Present	Absent	Present
≤5·5	2·39 (22)	1·81 (4)	2·30 (26)	
–6·5	2·40 (70)	2·23 (10)	2·38 (78)	2·39 (2)
–7·5	2·47 (163)	2·38 (25)	2·47 (175)	2·29 (13)
–8·5	2·53 (179)	2·33 (12)	2·53 (183)	2·40 (8)
–9·5	2·54 (103)	2·36 (5)	2·56 (103)	2·00 (5)
>9·5	2·57 (43)	2·36 (3)	2·57 (43)	2·30 (3)
All	2·50 (580)	2·30 (59)	2·49 (608)	2·28 (31)

CONCLUSIONS:

Lower birth weight was associated with worse adult lung function.

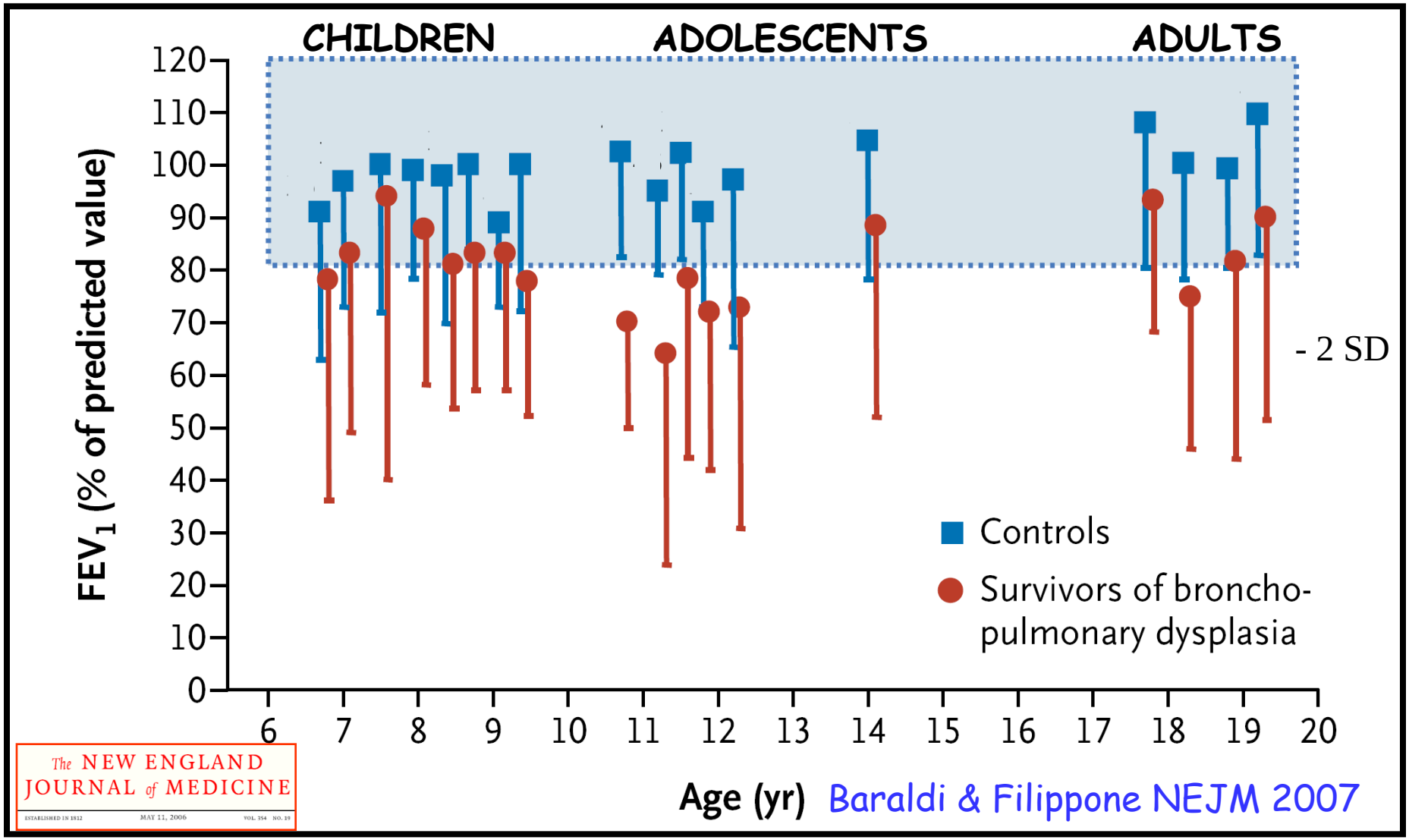
Intrauterine influences which retard fetal weight gain may irrecoverably constrain the growth of the airways.

Bronchitis, pneumonia, or whooping cough in infancy further reduced adult lung function. They also retarded infant weight gain.

Consistent with this, death from chronic obstructive airways disease in adult life was associated with lower birth weight and weight at 1 year.

Promoting lung growth in fetuses and infants and reducing the incidence of lower respiratory tract infection in infancy may reduce the incidence of chronic obstructive airways disease in the next generation.

STUDIES SINCE 1990 to 2006 in BPD SURVIVORS (age 6-19 years)



The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 11, 2006 VOL. 354 NO. 19

Risk Factors for COPD

Genes

Exposure to particles

- **Tobacco smoke**
- Occupational dusts, organic and inorganic
- **Indoor air pollution** from heating and cooking with biomass in poorly ventilated dwellings
- **Outdoor air pollution**

Lung growth and development

Gender

Age

Respiratory infections

Socioeconomic status

Asthma/Bronchial hyperreactivity

Chronic Bronchitis

Tobacco smoke

In utero exposure to cigarette smoking influences lung function at birth

K.C. Lødrup Carlsen, J.J.K. Jaakkola, P. Nafstad, K-H. Carlsen Eur Respir J 1997; 10: 1774–1779.

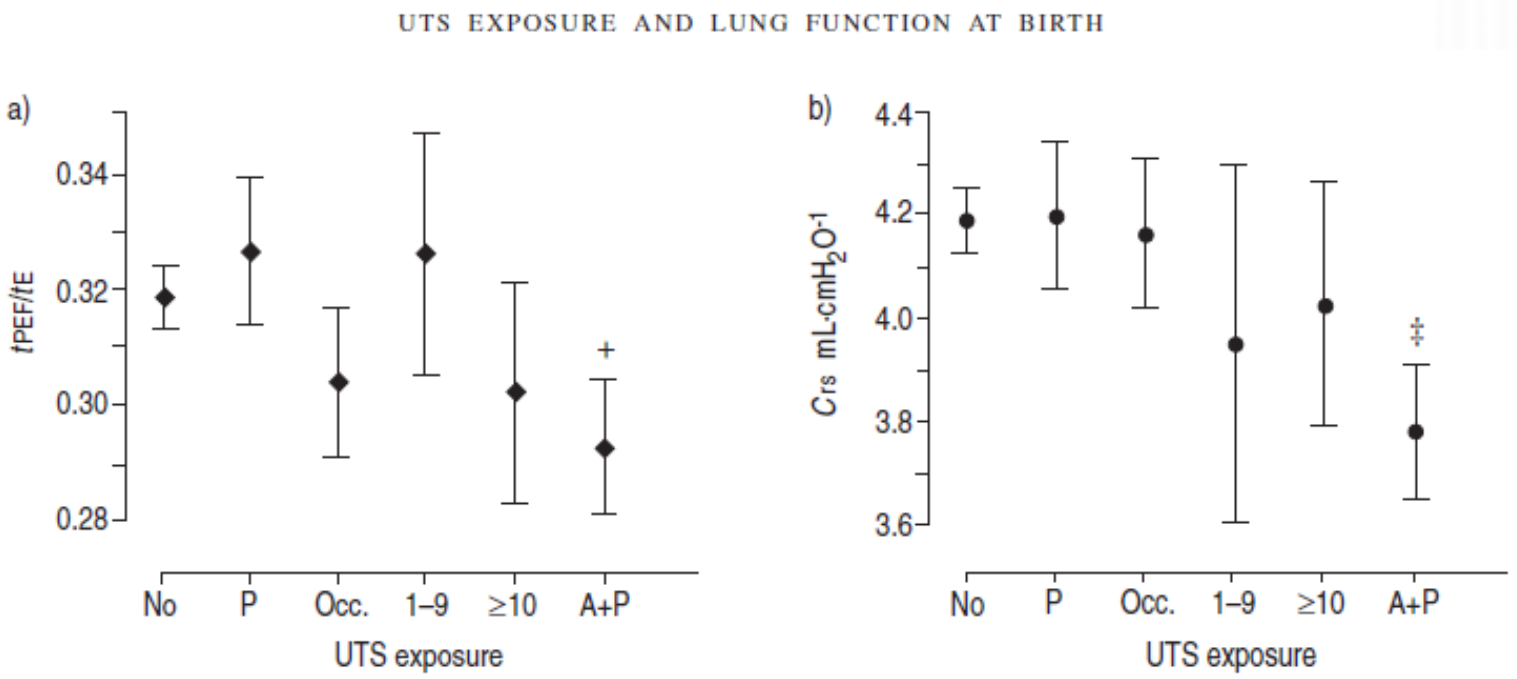
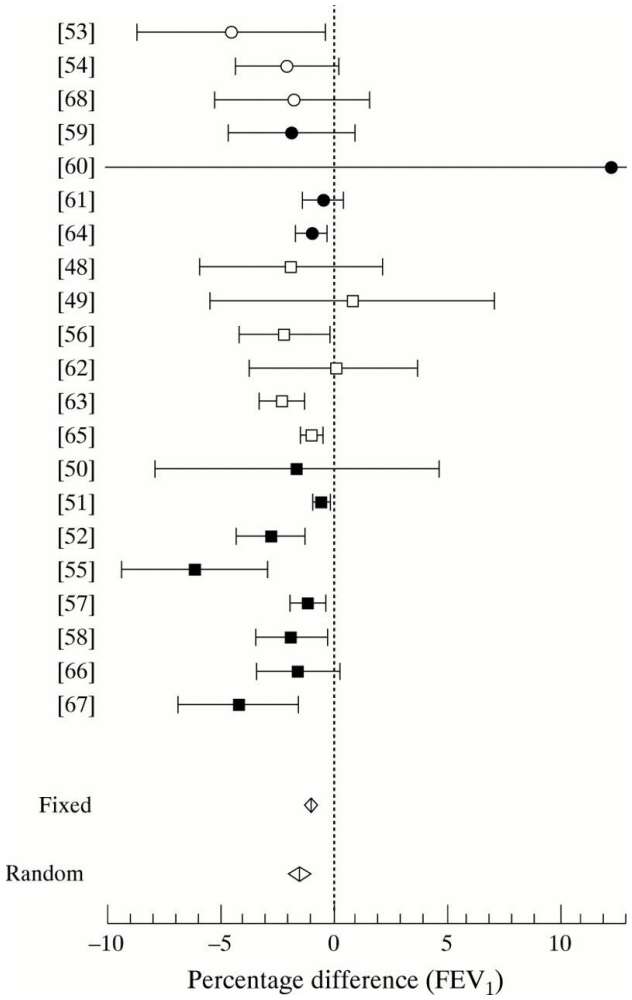


Fig. 1. – a) t_{PEF}/t_E; and b) C_{rs} in newborn babies in relation to maternal smoking. Values are presented as mean and 95% confidence interval. No: no active or passive maternal smoking; P: daily passive (but not active) maternal exposure to tobacco smoke in the household; Occ.: occasional maternal smoking (±passive smoking); UTS: uterine tobacco smoke exposure; 1–9: maternal active (but not passive) smoking of 1–9 cigarettes·day^{-1}; ≥10: maternal active (but not passive) smoking of ≥10 cigarettes·day^{-1}; A+P: both active and passive daily smoking. t_{PEF}/t_E: ratio of time to reach peak expiratory flow to total expiratory time; C_{rs}: compliance of the respiratory system. +: p=0.04; ‡: p<0.005, compared to nonexposed group.

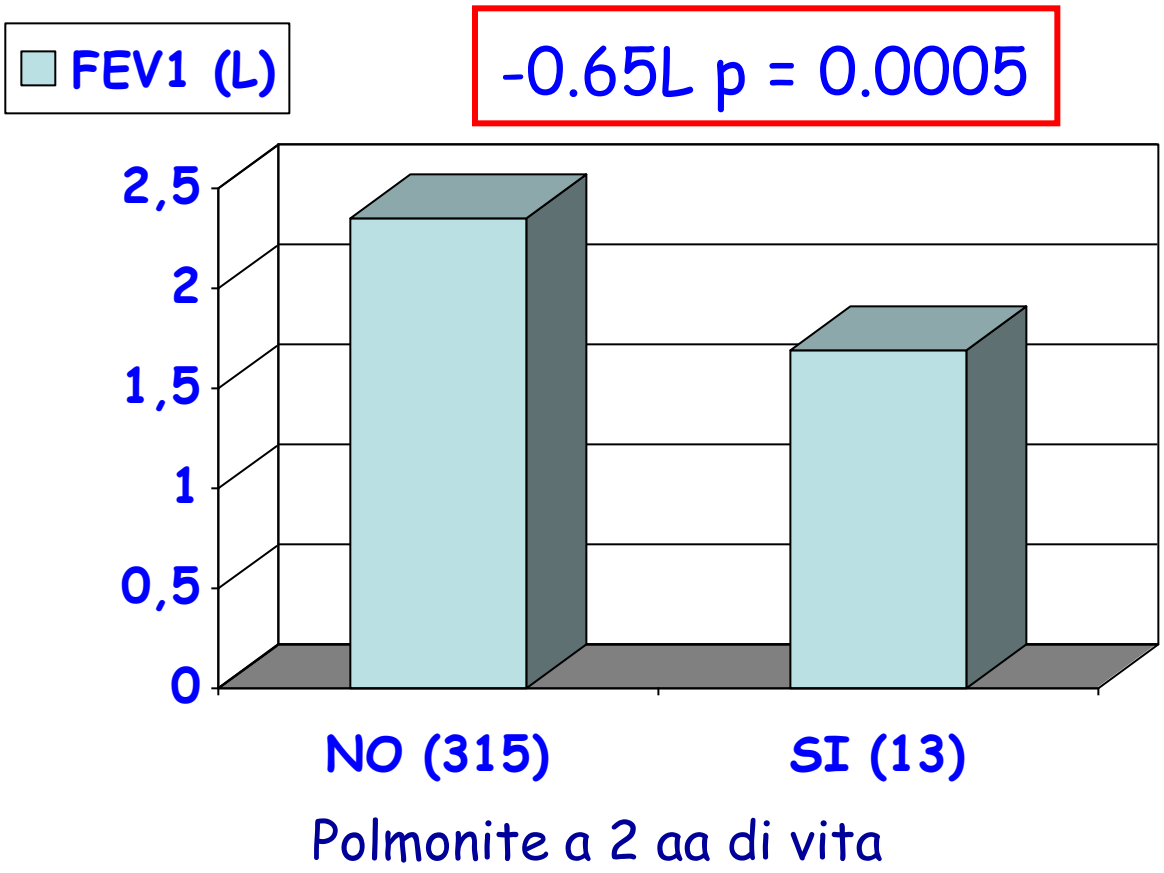
Health effects of passive smoking. Parental smoking and spirometric indices in children.

Cook DG, Strachan DP, Carey IM. Thorax. 1998 Oct;53(10):884-93.

Percentage difference in FEV1 between children of smokers and non-smokers from cross sectional studies:
open symbols are studies not adjusting for confounders other than age, height and sex; filled symbols are studies which adjusted for a variety of confounders.



INFEZIONI RESPIRATORIE



The relationship between pneumonia in early childhood and impaired lung function in late adult life.

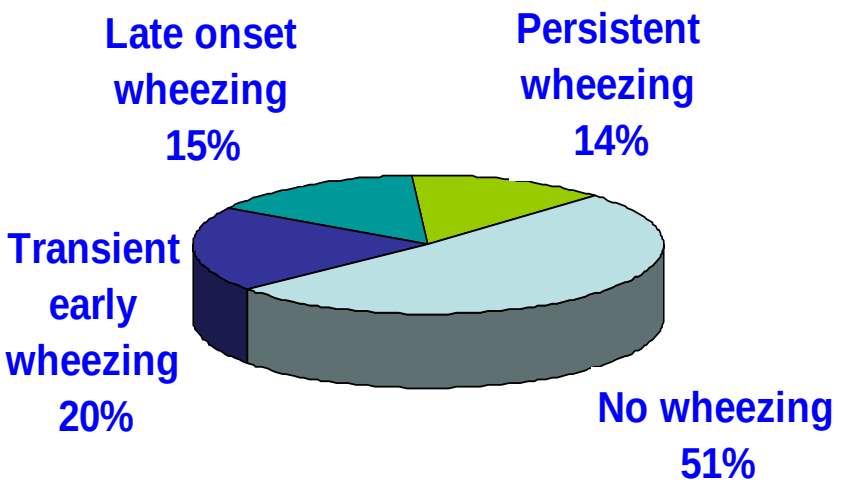
Shaheen SO, Barker DJ, Shiell AW, Crocker FJ, Wield GA, Holgate ST Am J Respir Crit Care Med. 1994 Mar;149(3 Pt 1):616-9


© Ron Niebrugge / WildNatureImages.com

Tutto iniziò da .. Tucson (almeno per noi pediatri)

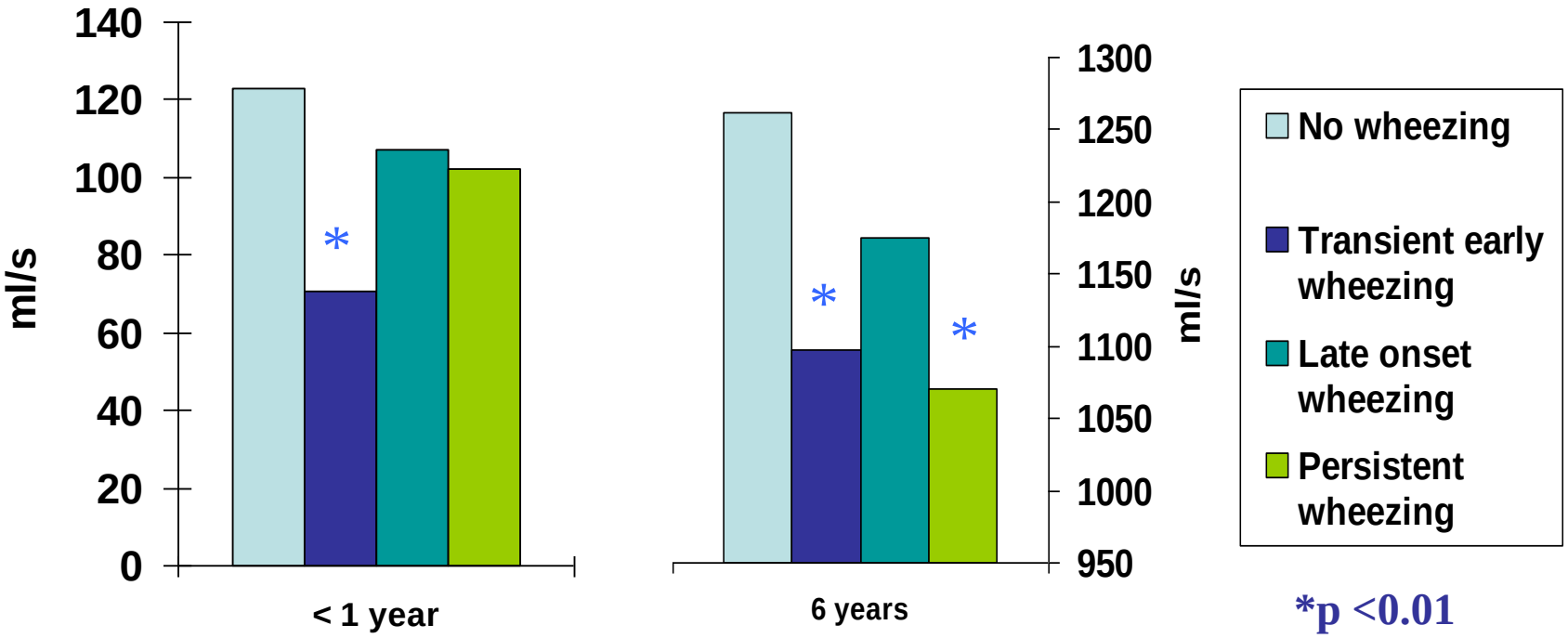
1246 neonati seguiti fino ai 3 anni e ai 6 anni di vita (826)

✓**Nel 1° anno di vita**
IgE cordone (n.750)
PFT a < 6 m (n.125)
IgE seriche 9m (n.672
✓ **A1 anno di vita**
Questionario (n.800)
✓ **Primi 3 anni**
follow-up per patologia basse vie aeree (n.888)
✓ **A 6 anni di vita**
questionario sul wheezing (n.1024)
✓ **A 6 anni di vita**
IgE seriche (n.460)
PFT (n.526)
Skin Tests (n.629)



Asthma and Wheezing in the First Six Years of Life
Fernando D. Martinez, et al. (N Engl J Med. 1995;332:133-8.)

VmaxFRC durante il 1 anno di vita e a 6 anni in funzione della storia di wheezing.



Asthma and Wheezing in the First Six Years of Life

Fernando D. Martinez, et al. (N Engl J Med. 1995;332:133-8.)

Asthma and Wheezing in the First Six Years of Life

F.D. Martinez, et al. (N Engl J Med. 1995;332:133-8.)

Transient Early wheezer

Associazione con fumo materno
Non correlazione con familiarità e atopia
Episodi correlati con flogosi alte vie
Funzione respiratoria alterata anche prima degli episodi
Funzione respiratoria alterata a 6 anni

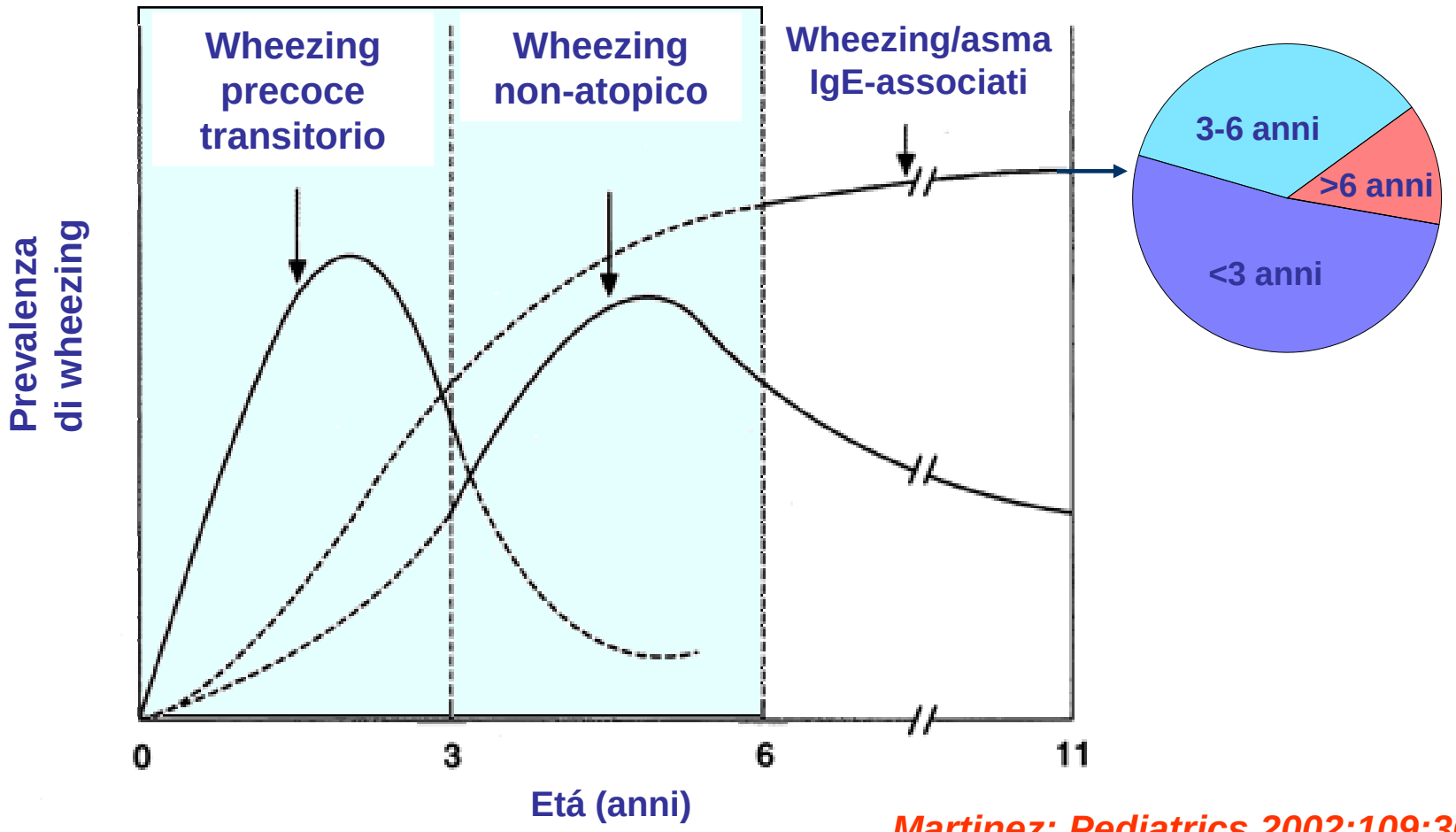
Late onset wheezer

Familiarità per asma e atopia
Sesso maschile
Skin test positivi
Funzione respiratoria normale

Persistent wheezer

Forte associazione con familiarità e atopia
Episodi di wheezing molto frequenti, anche senza associazione a flogosi alte vie
IgE e skin test alterati
Funzione respiratoria alterata a 6 anni.

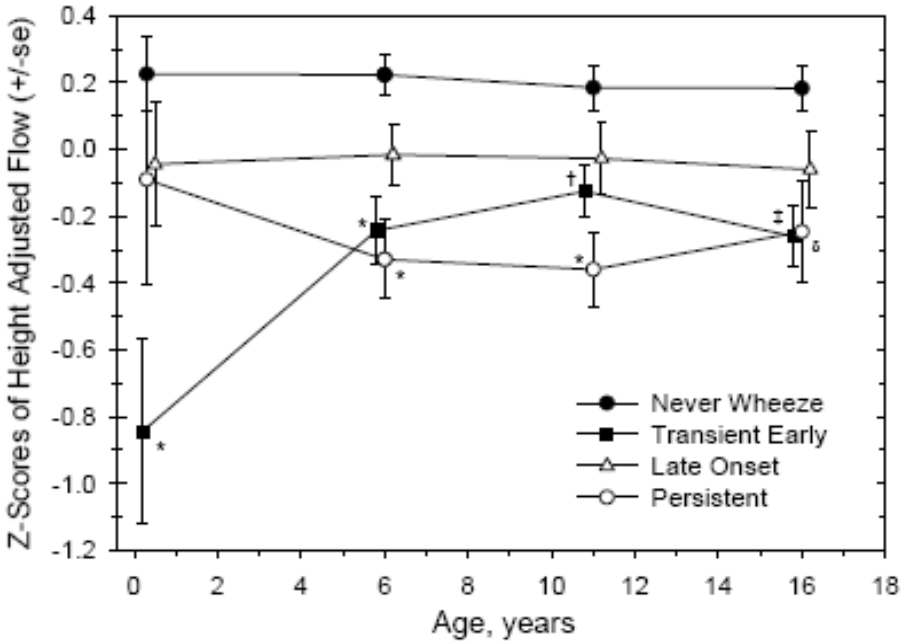
Differenti fenotipi di wheezing in età pediatrica e relativa prevalenza



Martinez: Pediatrics 2002;109:362

Outcome of Asthma and Wheezing in the First Six Years of Life: Follow-up through Adolescence.

Morgan WJ, Stern DA, Sherrill DL, Guerra S, Holberg CJ, Guilbert TW, Taussig LM, Wright AL, Martinez FD.
Am J Respir Crit Care Med. 2005 Aug 18; [Epub ahead of print]



Conclusion:

Patterns of wheezing prevalence and levels of lung function are established by age 6 and do not appear to change significantly by age 16 in children who start having asthma-like symptoms during the preschool years.

Storia Naturale dell'Asma Infantile

Panizzolo C., Barbato A.: Pneumologia Pediatrica 2004,13:38-42

Tabella 1 Principali studi di coorte che analizzano i fattori di rischio respiratorio dall'infanzia all'età adulta. *Coorte di pazienti asmatici selezionati non rappresentativi della popolazione generale.

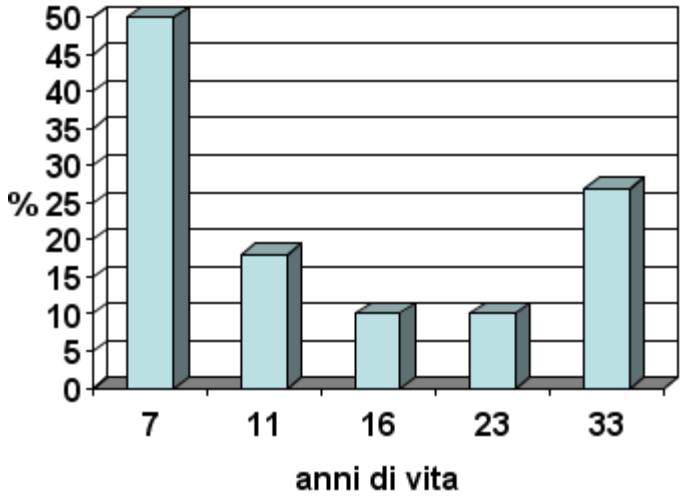
Sede	Anno d'inizio	Età d'inizio	Numero di soggetti all'inizio dello studio	Età adulti	Numero adulti
UK	1958	Nascita	17.414	23 33	14.571 5.801
Melbourne	1964	7 anni	401	28 35	323 327
Groningen* (Olanda)	1966-1969	5-14 anni	119	32-42	101
Tasmanie	1968	7 anni	8.683	29-32	1.723
Groningen* (Olanda)	1972-1976	8-12 anni	406	20-29	285
Poole (UK)	1976-1977	Nascita	100	22	63
Belmont (Australia)	1982	8-10 anni	718	23-27	498
Dunedin (Nuova Zelanda)	1972-1973	Nascita	613	26	613

R. Cutrera, 2012, cutrera@opbg.net

Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort.

Strachan DP, Butland BK, Anderson HR. BMJ. 1996 May 11;312(7040):1195-9.

- **Subjects**: 18 559 people born on 3-9 March 1958. 5801 (31%) contributed information at ages 7, 11, 16, 23, and 33 years
- **Main outcome measure**: History of asthma, wheezy bronchitis, or wheezing obtained from interview with subjects' parents at ages 7, 11, and 16 and reported at interview by subjects at ages 23 and 33
- **Results**: The cumulative incidence of wheezing illness was 18% by age 7, 24% by age 16, and 43% by age 33.
- 880 subjects developed asthma or wheezy bronchitis from birth to age 7



% degli 880 soggetti con asma prima dei 7 anni di vita con sintomi asmatici ancora presenti ai vari controlli

Le recidive a 33 anni erano fortemente associate con la presenza di atopia e il fumo attivo di tabacco

R. Cutrera, 2012, cutrera@opbg.net

Longitudinal study of childhood wheezy bronchitis and asthma: outcome at age 42

Horak E, Lanigan A, Roberts M, Welsh L, Wilson J, Carlin JB, Olinsky A, Robertson CF.
BMJ. 2003 Feb 22;326(7386):422-3.

Melbourne Study

- 1964: 401 bambini 7 anni (295 asma)
- 1967: 83 bambini 10 anni con asma grave

105 Controlli

74 Mild wheezy bronchitis (<5episodi di WARI)

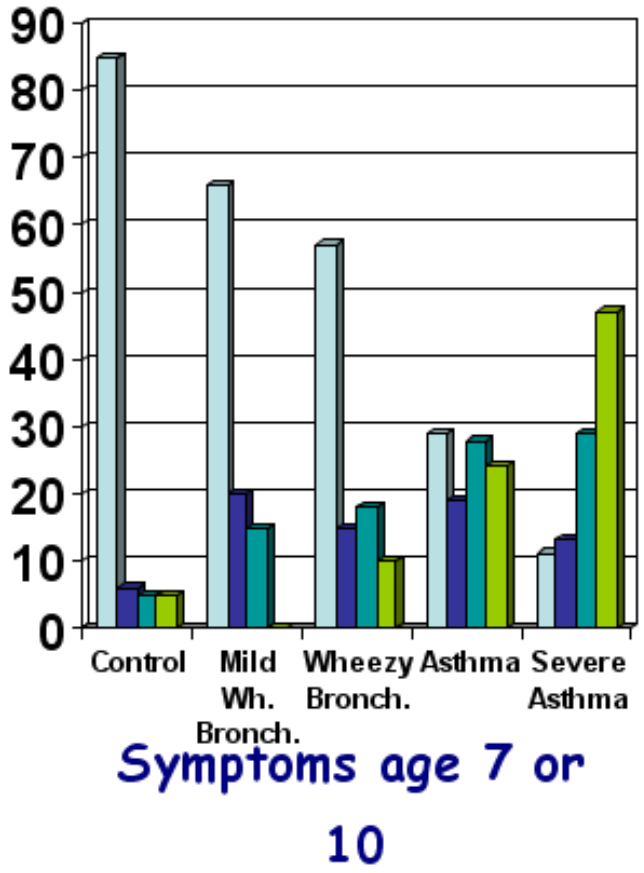
104 Wheezy bronchitis (>5episodi di WARI)

113 Asma (wheezing anche senza infezioni respiratorie)

83 Asma grave (inizio prima dei 3 aa, persistenza a 10 aa. Deformità toraciche o FEV1/FVC ≤ 50 %)

- A 42 anni: 15 morti (1 per asma)

403/464 partecipanti (87%)



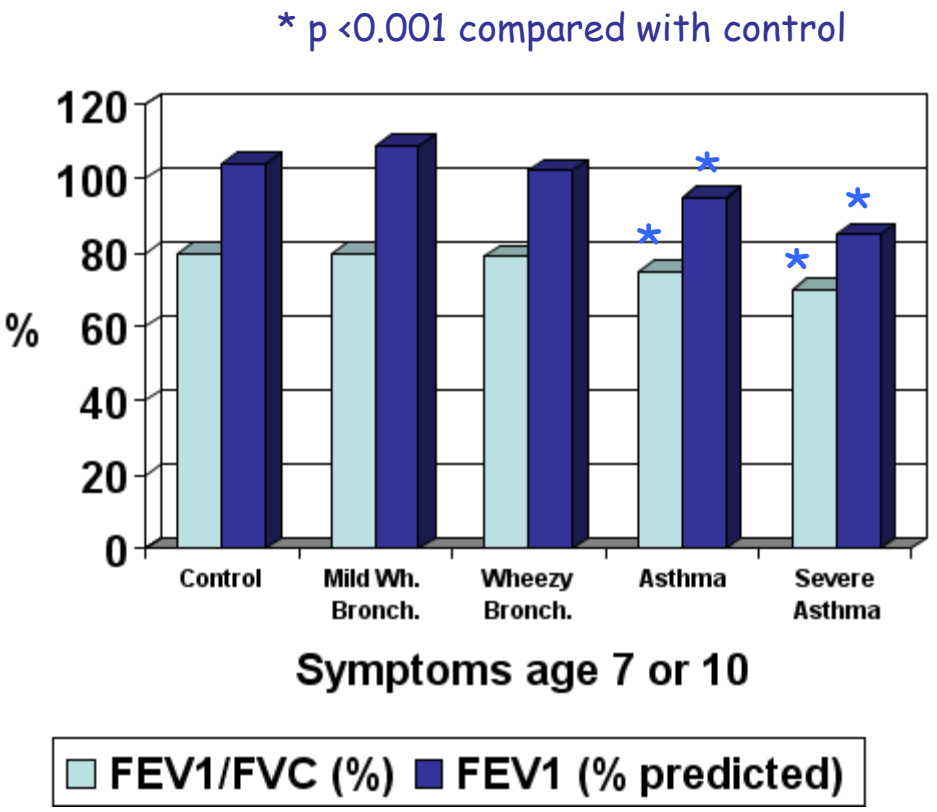
R. Cutrera, 2012, cutrera@opbg.net

Longitudinal study of childhood wheezy bronchitis and asthma: outcome at age 42

Horak E, Lanigan A, Roberts M, Welsh L, Wilson J, Carlin JB, Olinsky A, Robertson CF.
BMJ. 2003 Feb 22;326(7386):422-3.

At 42 years 267 participants attended at the laboratory for LFT

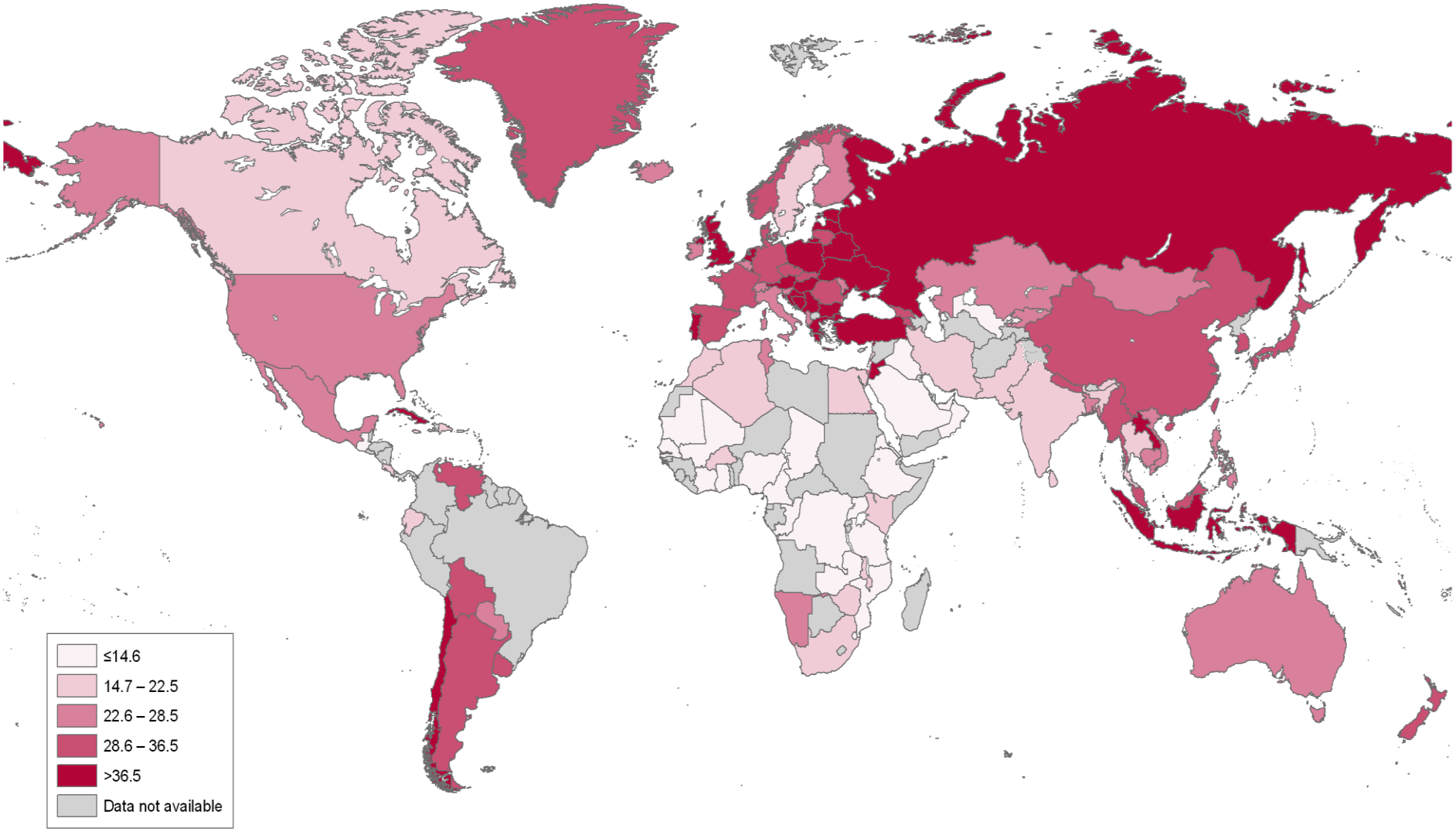
Our study shows that the pattern of asthma during childhood predicts outcome. Most children with persistent asthma had continuing symptoms into adult life and reduced lung function.



R. Cutrera, 2012, cutrera@opbg.net


Protect children: don't make them breathe your smoke

Percentage of tobacco use among adults, 2005



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Mapping and GIS
World Health Organization

World Health Organization

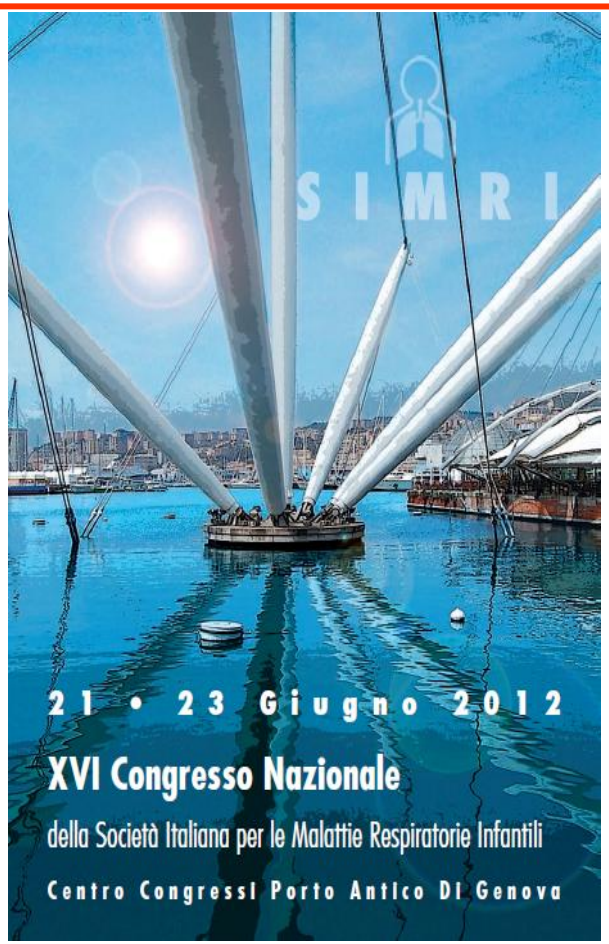
Conclusioni

La COPD è una malattia dell'adulto, ma le sue origini sono in età pediatrica

Il pediatra puo' fare molto:

- Migliorando la salute della madre e del bambino
- Riconoscendo e trattando le infezioni
- Curando al meglio l'asma del bambino
- Contribuendo a migliorare l'ambiente e sterno e interno del bambino
- Controllo del fumo di tabacco nei genitori
- Prevenzione del fumo di tabacco nel bambino e nell'adolescente

Consigli per… l'aggiornamento



Genova, 21-23 Giugno2012

Ischia, 4-7 Ottobre 2012

- Chronic obstructive pulmonary disease (COPD) is a life-threatening lung disease that interferes with normal breathing – it is more than a "smoker's cough".
- An estimated 64 million people have COPD worldwide in 2004.[1]
- More than 3 million people died of COPD in 2005, which is equal to 5% of all deaths globally that year.
- Almost 90% of COPD deaths occur in low- and middle-income countries.
- The primary cause of COPD is tobacco smoke (through tobacco use or second-hand smoke).
- The disease now affects men and women almost equally, due in part to increased tobacco use among women in high-income countries.
- COPD is not curable, but treatment can slow the progress of the disease.
- Total deaths from COPD are projected to increase by more than 30% in the next 10 years without interventions to cut risks, particularly exposure to tobacco smoke.