



**VIII CONGRESSO
REGIONALE
FIMP MARCHE**

La Scienza

e la

Professione

Hotel Conero Break

Via Luigi Albertini n. 6 - 60131 Ancona

Ancona, 21 ottobre 2017

La gestione del bambino con
patologia respiratoria cronica

Salvatore Cazzato

UO Pediatria

Presidio Ospedaliero di Alta Specializzazione "G. Salesi"

Azienda Ospedaliero-Universitaria

Ospedali Riuniti di Ancona

Prevalenza **OSAS** 1-5%
popolazione pediatrica



10-20%

- **Picco di incidenza tra i 2 e i 8 anni**
periodo di massima iperplasia tessuto linfatico
- **M:F=1:1**

20%

Russatori abituali

PSG +ve

Sindrome delle apnee ostruttive nel sonno (OSAS)

Am J Respir Crit Care Med 1996;153;866-78.

Disturbo respiratorio che si verifica durante il sonno caratterizzato da

- episodi prolungati di **ostruzione parziale (ipopnea)**
- e/o
- **ostruzione completa (apnea ostruttiva)** intermittente **delle alte vie aeree**



Alterazione della ventilazione notturna
e
architettura del sonno



Fattori di rischio per OSAS

- Ipertrofia adeno-tonsillare
- Obesità
- Anomalie cranio-faciali
- Disordini neuromuscolari

Complicanze sistemiche OSAS non trattata

- Disturbi cognitivi e comportamentali
 - deficit di apprendimento e di concentrazione
 - Iperattività /aggressività
- Compromissione dell'accrescimento staturo-ponderale
- Ipertensione sistemica
- Ipertensione polmonare
- Ipertrofia cardiaca (IVD)



sintomi/segni clinici

Sintomi notturni

- russamento abituale o respiro rumoroso (>95%)
- apnee
- rientramenti al giugulo ed intercostali (+severe)
- sudorazioni profuse nel sonno
- bere durante la notte (respirazione orale)
- risvegli improvvisi che possono simulare il pavor nocturnus

Sintomi diurni

- secchezza della bocca
- cefalea mattutina
- Iperattività/irritabilità
- deficit dell'attenzione (con conseguente scarso rendimento scolastico)

Esame fisico

- *presenza di ostruzione nasale*
- presenza e grado di ipertrofia adeno-tonsillare
- *pattern di crescita*
- morfologia del palato (palato ogivale)
- obesità
- presenza di dimorfismi cranio-facciali (micrognazia/retrognazia/craniosinostosi)



Fenotipo classico

- **facies adenoidea**

volto allungato

occhi alonati

respirazione orale

naso insellato

palato ogivale

- tonsille ipertrofiche

- **ritardo di accrescimento staturo ponderale**

- *pectus excavatum*



FENOTIPO *ADULT TYPE*



obesità

Area pediatrica 2005

FENOTIPO CONGENITO



micrognazia, ipoplasia mandibolare, retrognazia,
anomalie craniofacciali complesse (es. Pierre-
Robin,

NELLA PRATICA CLINICA...

Russamento primario



OSAS

La maggior parte dei bambini affetti da OSAS presenta russamento notturno

Tuttavia **non tutti i bambini che russano** presentano OSAS
(solo il 10-30% di questi presenta OSAS, documentata alla polisonnografia)

Alkhalil M et al, Pediatric obstructive sleep apnea syndrome (OSAS) for the allergist: update on the assessment and management, Ann Allergy Asthma Immunol 2011

Storia ed esame fisico

- visita pediatrica di routine dovrebbe comprendere sempre **una storia clinica** riguardante il sonno ed il russamento.
 - **non sufficiente a distinguere il russamento primario dall'OSAS**



selezionare i bambini che devono continuare il percorso diagnostico

– **Scarsa sensibilità e specificità**

- » Marcus CL et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2012
- » Pediatrics 2002; 109: e69

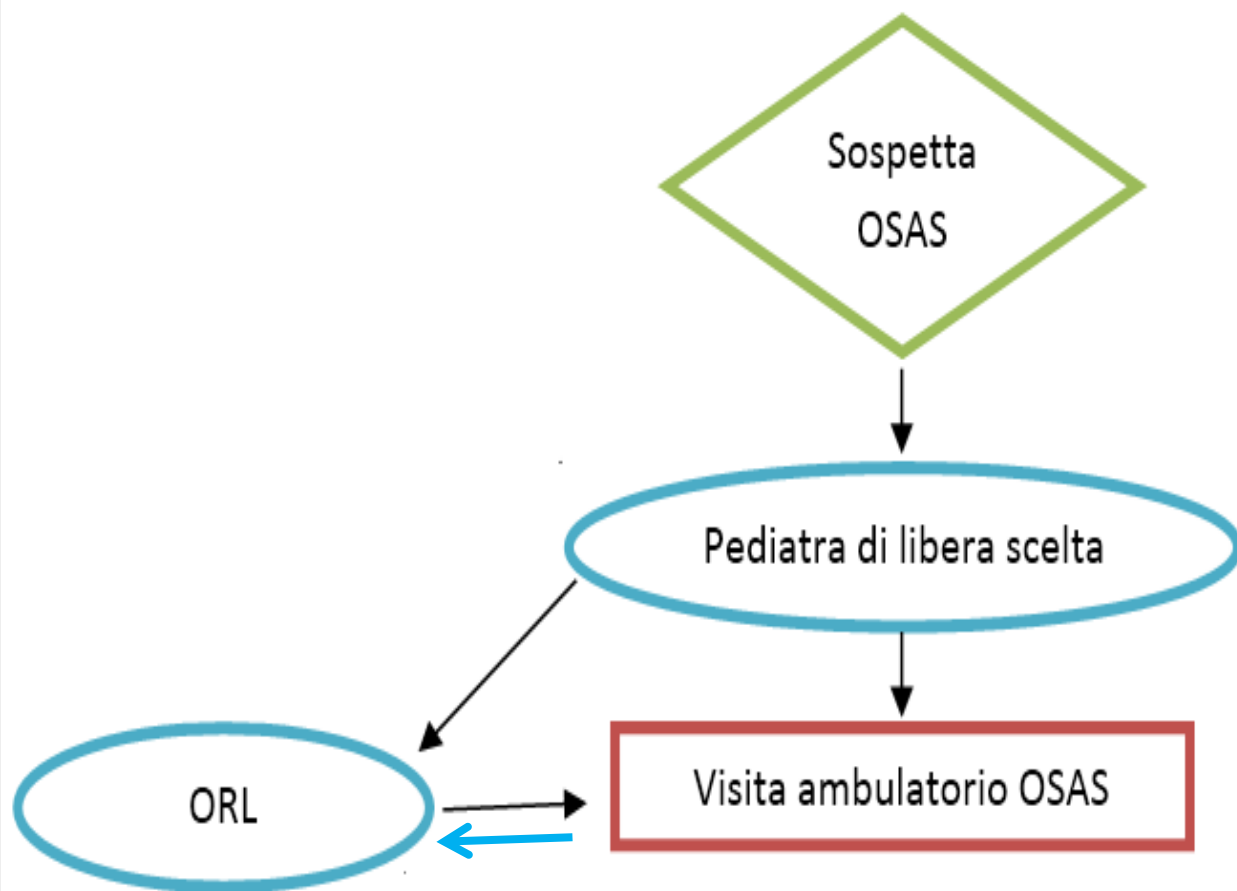
storia clinica ed esame fisico hanno un valore predittivo positivo per la diagnosi di OSAS rispettivamente del 65% e 46%.

OSAS metodi di diagnosi

Registrazione Audio/Registrazione video

- non in grado di distinguere il russamento primario dal russamento associato ad OSAS
- non definiscono la **severità (priorità intervento)**
- utile come screening

Eur. Respir. J. 1996; 9: 2127–31
Pediatr. Pulmonol. 1999; 27: 267–72



Visita ambulatoriale



Screening per OSAS: verificare
-se russamento abituale e persistente (3
volte/sett da almeno 2 mesi)
+
segni o sintomi di OSAS

+



Centro del sonno
(Pneumologia Pediatrica)

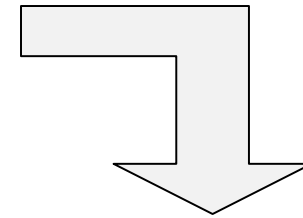
ORL

polisonnografia +



**Conclusioni
diagnostiche
condivise e terapia**

PSG non disponibile



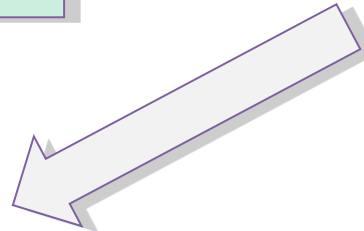
elevata probab
pre-test

-ve



pulsossimetria

+ve



Rischio di complicanze postoperatorie

(indicazione all'assistenza in Terapia Intensiva)

- **Bambini di età < 3 anni**

- **OSAS di grado severo**

(scarso accrescimento, ipertrofia ventricolare destra, storia di prematurità)

- **Anormalità craniofacciali/m. neuromuscolari**

- **Sindrome di Down**



Polisonnografia notturna standard

(fortemente raccomandata)

PULSOSSIMETRIA NOTTURNA

Semplicità di esecuzione
anche a **domicilio**

Basso costo

Elevato valore predittivo
positivo (97%)

VPN 47%

Polisonnografia standard notturna

esame *gold standard*

Marcus al. Pediatrics 2012

- registrazione simultanea di più parametri fisiologici durante la notte
- stabilire la severità dei DRS

Parametri respiratori

Flusso oronasale

Movimenti toraco-addominali

Ossimetria

Parametri non respiratori

Elettroencefalogramma (EEG)

Elettrooculogramma-EOG

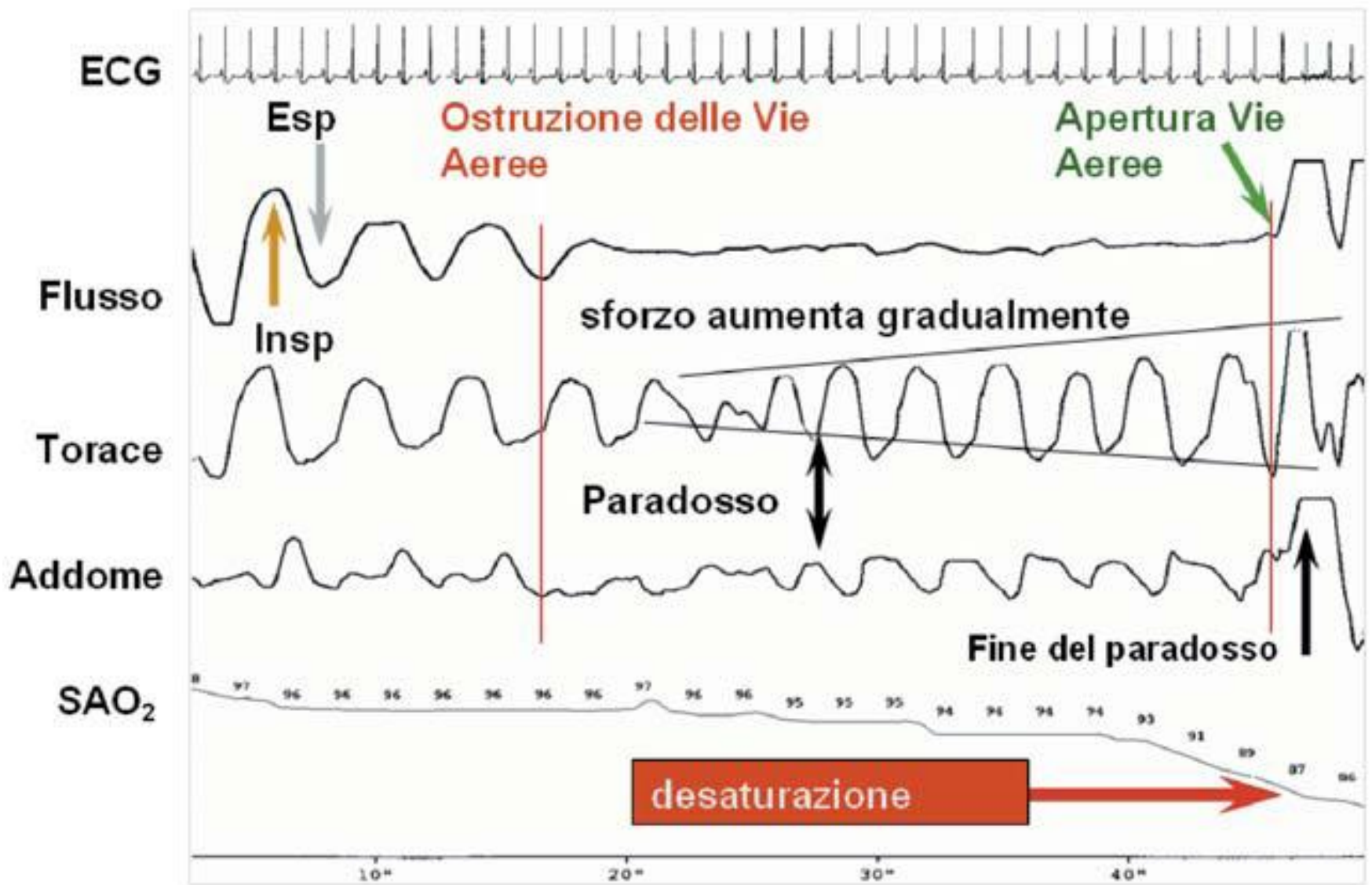
Elettromiogramma-EMG

Elettrocardiogramma-ECG

Rumore respiratorio

Montoraggio video

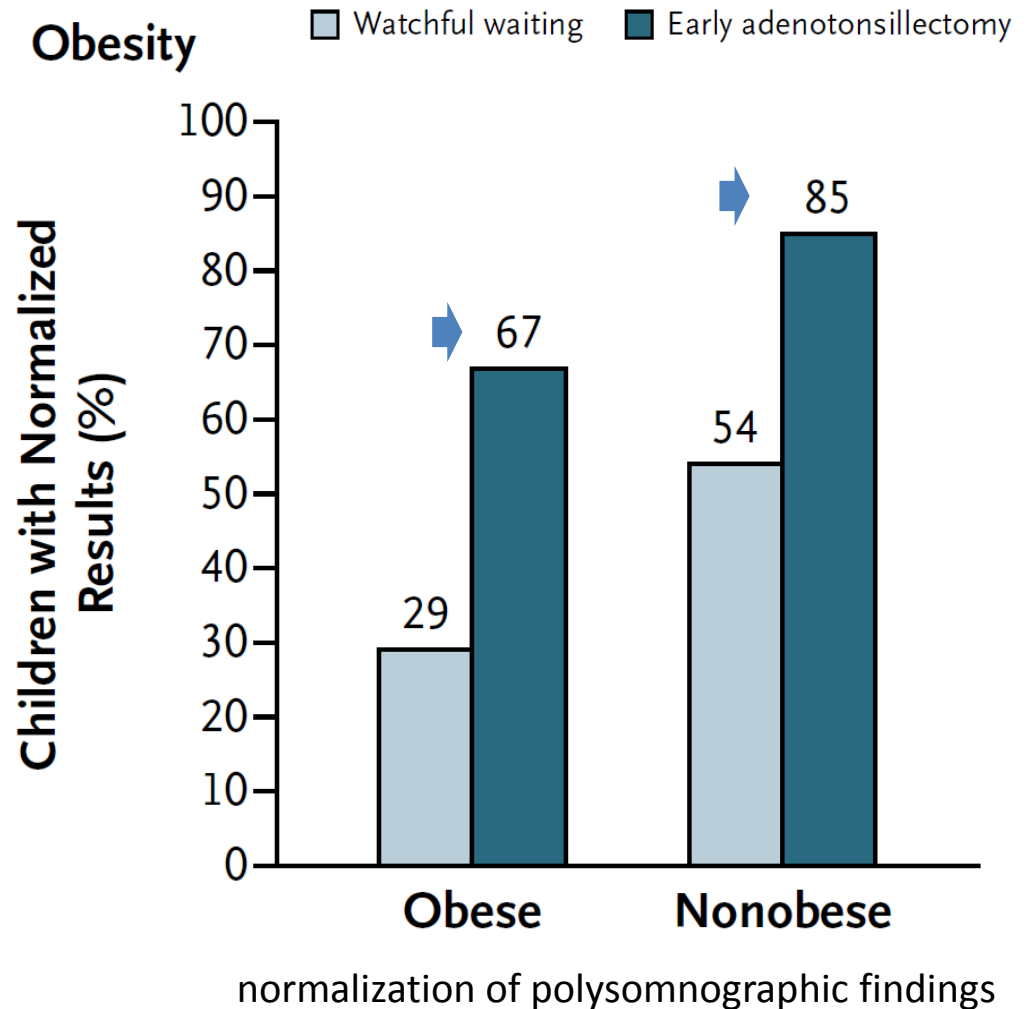
registrati vari canali EEG ed elettromiografici, i movimenti di torace e addome, il flusso oro-nasale, e la saturazione di ossigeno nel sangue.



Sindrome delle apnee ostruttive nel sonno in età pediatrica. Area Pediatrica 2005

A Randomized Trial of Adenotonsillectomy for Childhood Sleep Apnea

- randomly assigned 464 children, **5 to 9 years** of age, with the obstructive sleep apnea syndrome to early adenotonsillectomy or a strategy of watchful waiting.
- outcomes were assessed at baseline and at 7 months



Indications for polysomnography in a child suspected to have obstructive sleep apnoea (OSA)

MJA 2013; 199: S31–S35

Identification of severe OSA

Conditions with increased surgical risk that should have documentation of disease severity

Complex medical conditions such as Down syndrome, neuromuscular disorders and craniofacial syndromes

Age < 3 years

Persistence of symptoms after adenotonsillectomy

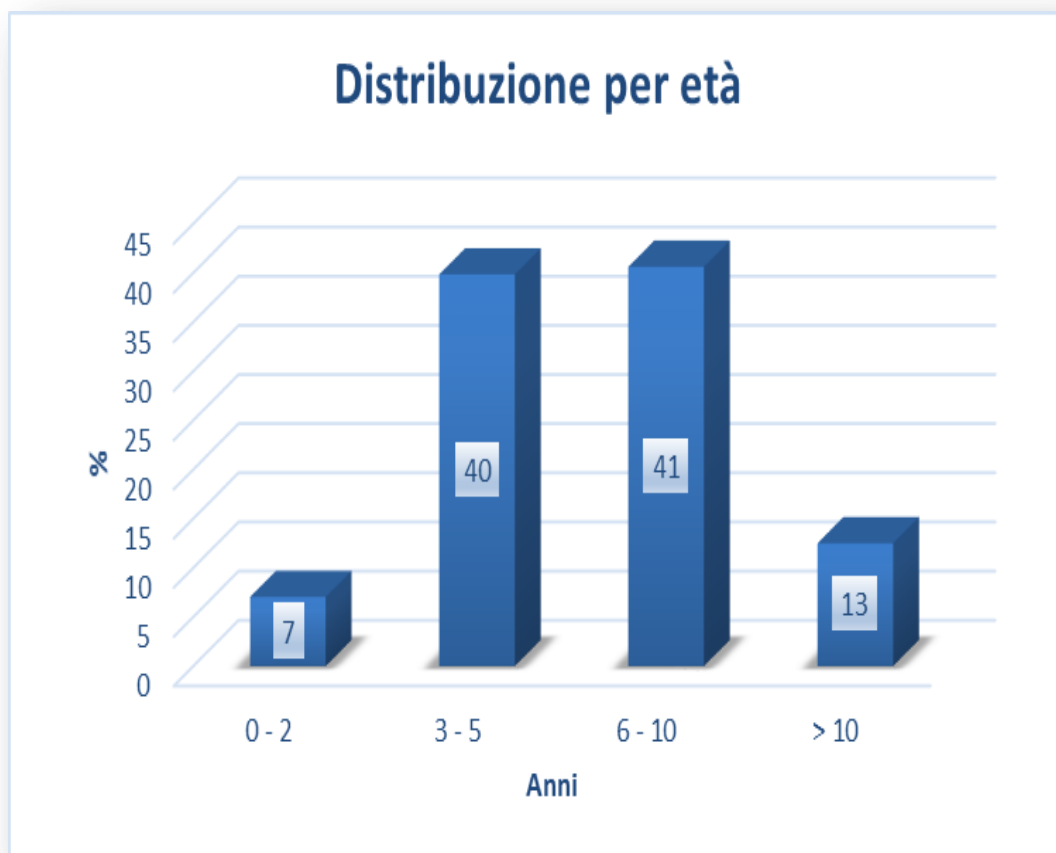
High-risk groups for persisting OSA:

**severe initial disease;
obesity;**

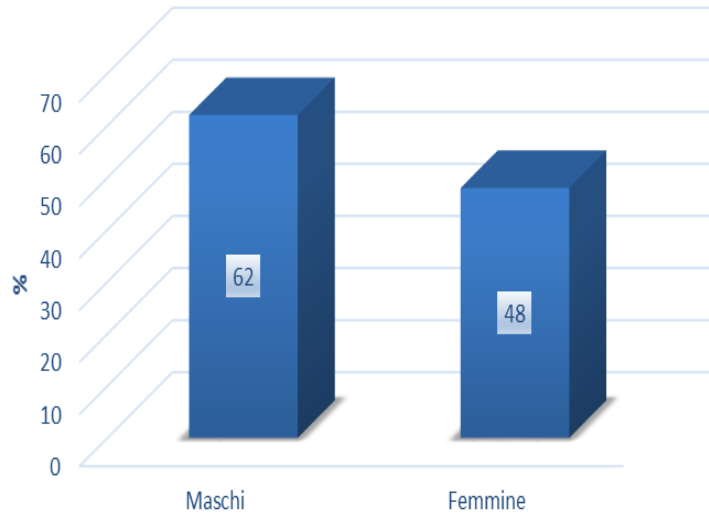
history of prematurity;
congenital syndrome/malformation;
atopy;

Ambulatorio disturbi respiratori del sonno (SOD Pediatria AN): attività gennaio – ottobre 2017

Visite ambulatoriali: 168



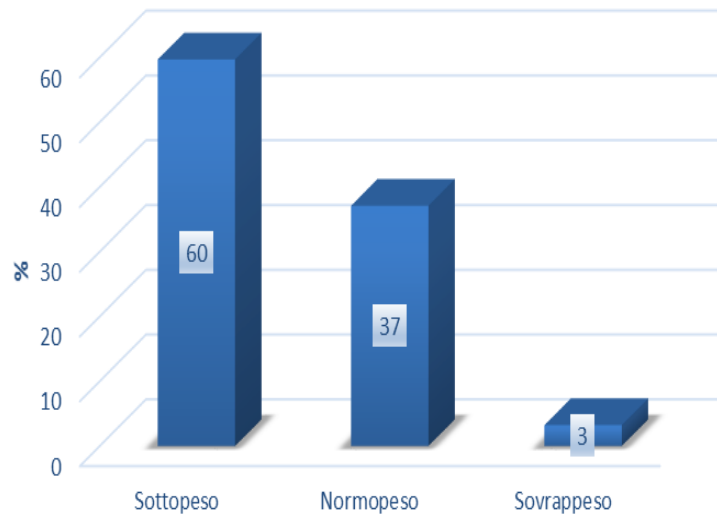
Sesso



Caratteristiche della popolazione

Prevalenza > nel sesso maschile

BMI



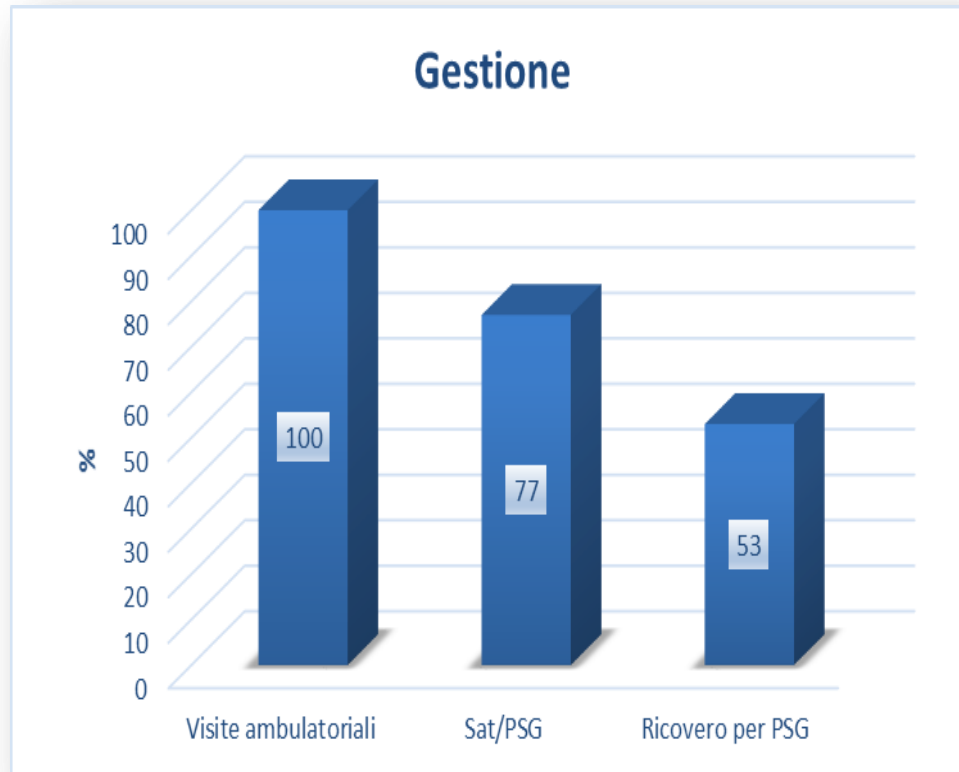
Prevalenza fenotipo “**adenoido**”:

- associazione con *Failure to Thrive*

Scarsa rappresentanza fenotipo “**obeso**”

**Ambulatorio disturbi respiratori
del sonno (SOD Pediatria AN):
attività gennaio – ottobre 2017**

Percorso diagnostico



La maggior parte dei pazienti valutati in ambulatorio eseguirà **approfondimenti strumentali**

Più della metà dei pazienti verrà valutata in **ricovero** per esecuzione PSG (con esami ematochimici, SPT, ...)

Es. saturimetrico

...

La maggior parte verrà indirizzata ad **esecuzione PSG** per miglior definizione della gravità dell'OSAS

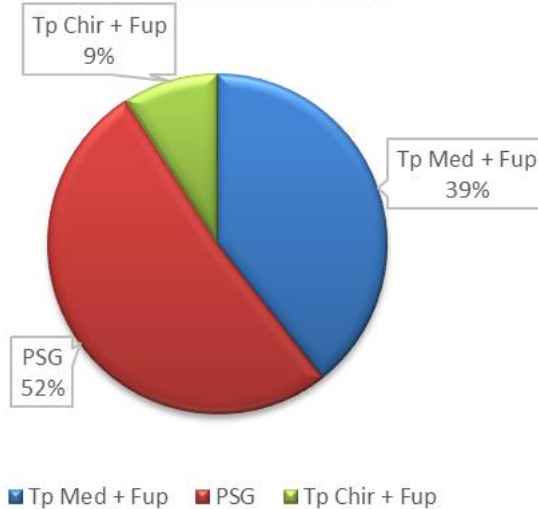
Quadri estremamente **severi**:

- Intervento chirurgico in tempi brevi (con indicazioni monitoraggio)

Quadri **normali/estremamente lievi**:

- Trial con terapia medica (+ follow-up)

Esito Saturimetria



PSG

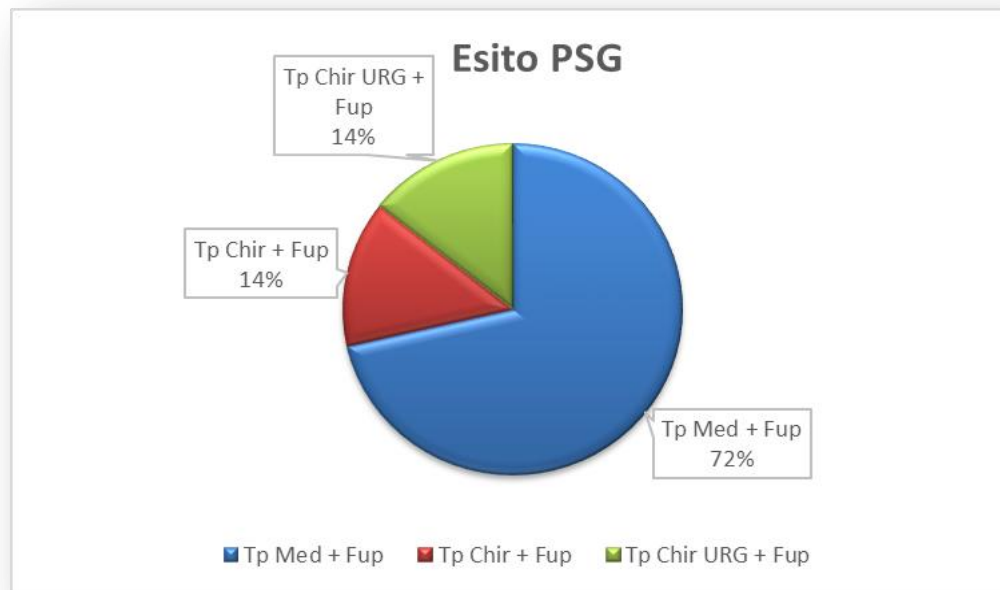
Ottimale **stratificazione** severità

$\frac{1}{3}$ dei pazienti → **chirurgia**

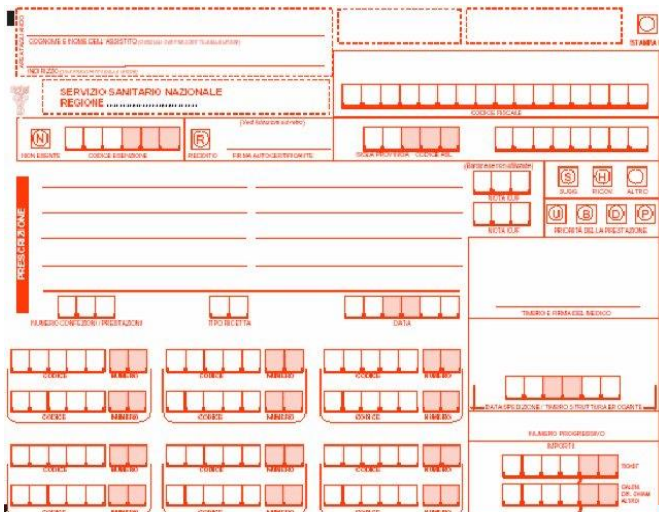
- di cui il 50% in regime di urgenza

Fondamentale **follow-up**:

- Efficacia trial terapia medica
- Eventuale OSAS residua dopo chirurgia



Alcune Informazioni utili!



Presidio Ospedaliero di Alta Specializzazione "G. Salesi"

Dipartimento Materno-Infantile

Telefono: 071 5962071

Email: pediatriasalesi@ospedaliriuniti.marche.it

È possibile accedere all'ambulatorio con la richiesta di:

- Visita Pneumologica Pediatrica (1°v/ctr)
- Visita Allergologica Pediatrica (1°v /ctr)
- Visita Pediatrica per DRS/OSAS

Prenotando al CUP regionale – tel. 800 098 798

Per i contatti diretti si può ricorrere al numero 071-5962071 tutte le mattine (lun-ven. 8:00-14:00).

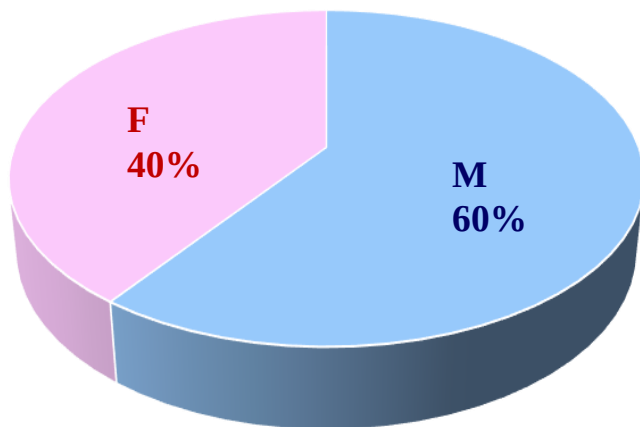
È inoltre attivo il servizio mail:

pediatriasalesi@ospedaliriuniti.marche.it

S.O.D. Pediatria
Direttore: Dott. Salvatore Cazzato

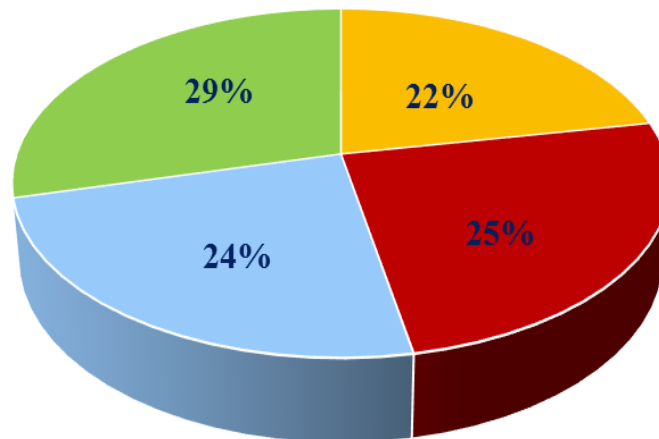
Dal 01/gennaio al 30 settembre 2017 sono state effettuate presso il ns Centro di Pneumologia e Allergologia Pediatrica oltre 2400 visite specialistiche:

Distribuzione per sesso (%)



■ Maschi ■ Femmine

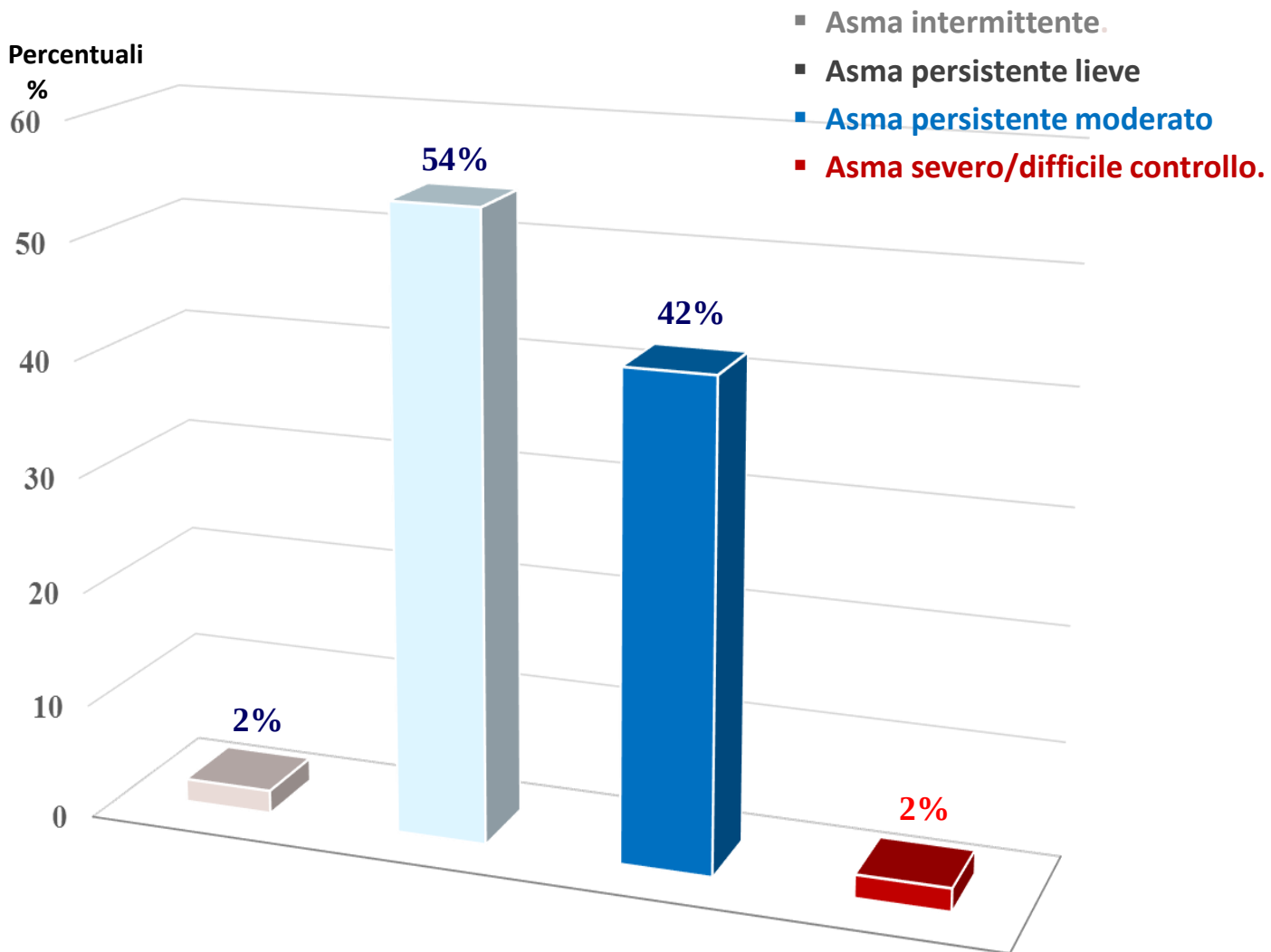
Distribuzione per fasce di età (%)

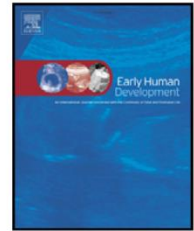


■ 0-3 anni ■ 4-6 anni ■ 7-10 anni ■ > 10 anni



Valori Percentuali





Interstitial lung disease in children[☆]

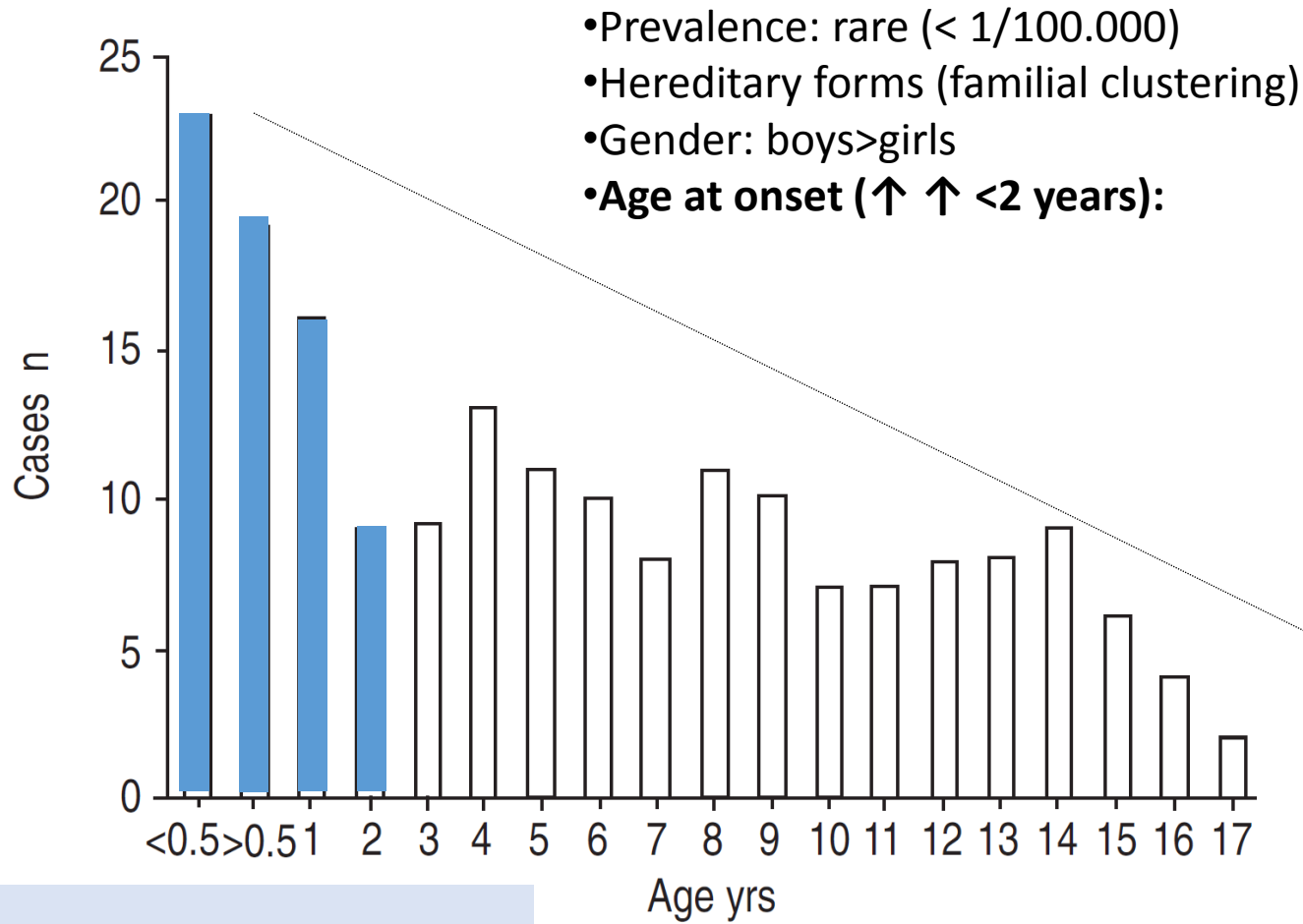


Salvatore Cazzato^{a,*}, Emanuela di Palma^a, Vincenzo Ragazzo^b, Silvia Ghione^c

- Diffuse lung diseases in children comprise a **heterogeneous** group of **rare** pediatric disorders
 - remodeling of the lung interstitium and distal airspaces
 - abnormal gas exchange

Interstitial lung disease in children

Epidemiology



ILD defined as:

respiratory symptoms and/or diffuse infiltrates on chest radiographs, Impaired gas exchange, persistence of any of these findings for > 3 months

Children's DLD requires the presence of **at least 3 of the following 4 criteria** in the absence of other known disorders:

1. Respiratory symptoms

- (cough, rapid and/or difficult breathing, or exercise intolerance)

2. Respiratory signs

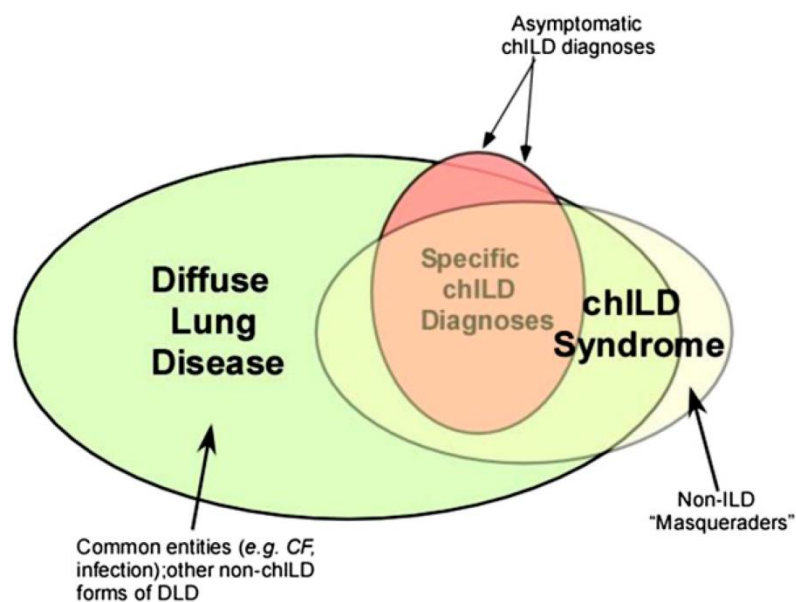
- (tachypnea, adventitious sounds, retractions, digital clubbing, failure to thrive, or respiratory failure)

3. Hypoxemia

4. Diffuse chest infiltrates on chest X-ray or CT scan

Abnormalities in PFT are not included, because they may not be available, particularly in younger children.

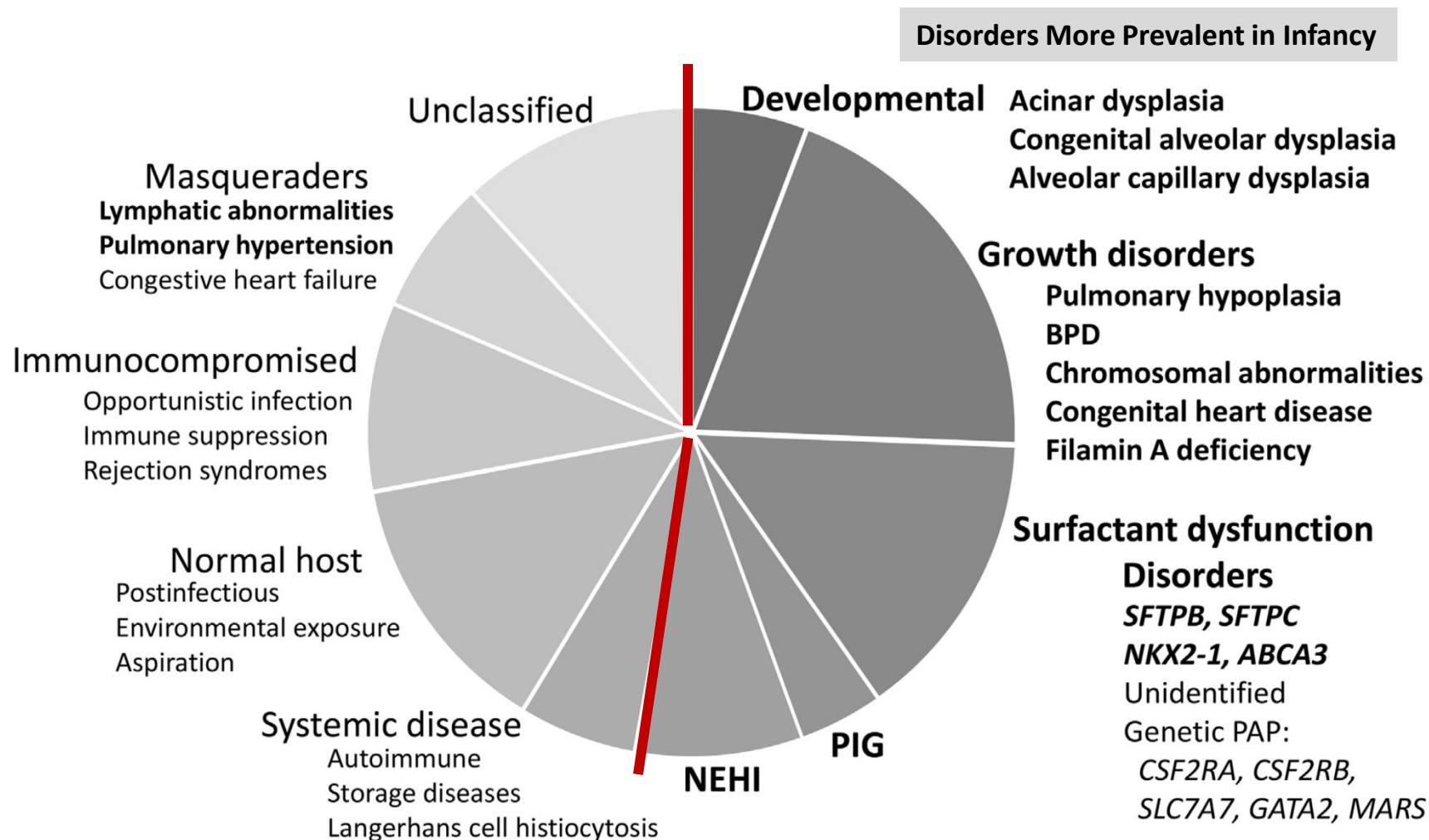
The chILD syndrome requires exclusion of the more common causes of DLD



- cystic fibrosis
- congenital or acquired immunodeficiency
- congenital heart disease
- bronchopulmonary dysplasia
- pulmonary infection
- primary ciliary dyskinesia presenting with newborn respiratory distress
- recurrent aspiration

Distribution of diagnoses of interstitial lung disease

Disorders and diagnoses in **bold type** are those more likely to present in the newborn period



Disorders not Specific to Infancy

Seminars in Fetal & Neonatal Medicine 2017

ARTICLE

Peca D, .. Cazzato S.. et al. European Journal of Human Genetics 2015

Clinical and ultrastructural spectrum of diffuse lung disease associated with surfactant protein C mutations

Case	Sex, gestational age, birth weight, family history	Presentation and clinical course	HRCT imaging	Treatment and outcome	ProSP-C expression and amyloid staining	Ultrastructure
1	F; term; 3.30 Kg Parents and one sibling healthy	Dyspnea and failure to thrive at 1 m PICU from 3 m Lung biopsy 3 m	3 m: ground glass opacities, upper lobes cysts, upper lobar emphysema, PTX	O ₂ from 1 m, MV from 3 m PS+HCQ from 3 m <u>Death 6 m</u>	AEC2 hyperplasia Granular proSP-C pattern with diffuse large aggregates Several amyloid deposits	Many large endosomes Very rare LBs with abnormal PL structure
2	M; term; 3.70 Kg Parents healthy, no siblings	Multiple bronchiolitis episodes 3–12 m Hypoxemia from 14 m PICU from 14 m Lung biopsy 18 m	14 m: ground glass opacities, multifocal interstitial infiltrates	O ₂ from 14 m, MV from 15 m, tracheostomy 16 m PS+HCQ from 15 m <u>Death 19 m</u>	Marked AEC2 hyperplasia Granular proSP-C pattern with diffuse large aggregates No amyloid detected	Many large endosomes with some PL content Very rare immature LBs and MVBs
3	M; term; 3.00 Kg Healthy parents and sister	Bronchiolitis 5 m PICU 9–13 m for respiratory failure, recurrent PTX Lung biopsy 15 m	9 m: ground glass opacities, multiple cysts	O ₂ from 11 m, MV 9–11 m PS+HCQ from 13 m Alive on O ₂ at 48 m <u>Listed for transplant</u>	AEC2 hyperplasia Granular proSP-C pattern with diffuse large aggregates No amyloid detected	Many large endosomes with PL content Very rare LBs
4	F; term; 3.30 Kg 1 sibling, fatal respiratory failure 16 m	Chronic cough and dyspnea since 7 m PICU 18–19 m for hypoxemia and dyspnea	10 m: diffuse ground glass opacities, honeycombing, multiple subpleural nodules.	O ₂ 18–21 m HCQ from 21 m <u>Alive on room air at 30 m</u>	n/a	n/a
5	M, Term, 2.990 Kg Parents healthy, no siblings	Chronic cough, failure to thrive since 9 m Hospitalized 13–14 m for dyspnea and hypoxemia	13 m: diffuse ground glass opacities	O ₂ 13–19 m Steroids for 5 m at 13 m AZM 18 m, HCQ from 13 m <u>Alive on room air at 21 m</u>	n/a	(tracheal aspirate) Some large endosomes with PL content Rare MVBs
6	F; term; 3.03 Kg Parents healthy, no siblings	Hospitalized for bronchiolitis at 6 m Hospitalized 11–15 m for hypoxemia and PTX, lung biopsy at 14 m	6 m: diffuse ground glass opacities, basal emphysema	O ₂ since 13 m, MV 6–7 m PS 11–12 m HCQ from 16 m <u>Alive on O₂ at 24 m</u>	Marked AEC2 hyperplasia Some granular proSP-C pattern plus perinuclear aggregates Rare amyloid deposits	Numerous mitochondria, lysosomes and electron-dense deposits Several normal LBs Several MVBs
7	F; term; 3.00 Kg Parents healthy, no siblings	Pneumonia at 1 y, Several hospitalizations for LRTI in childhood; severe failure to thrive Hypoxemia at 26 y	26 y: mild interstitial lung disease, diffuse tubular and varicose bronchiectasis, basal infiltrates	Intermittently on O ₂ , never ventilated Multiple antibiotic and PS courses, bronchodilators <u>Alive at 28 y on O₂</u>	n/a	n/a
8	M; 28 w; 0.90 Kg Parents healthy, two triplet siblings with no CLD	Severe RDS at birth, 2 doses of surfactant, MV until 4 w	2 m: diffuse ground glass opacities, overexpansion, bronchial markings	O ₂ 2–4 m, MV 1 m Steroids 1 m <u>Alive on room air at 14 m</u>	n/a	n/a

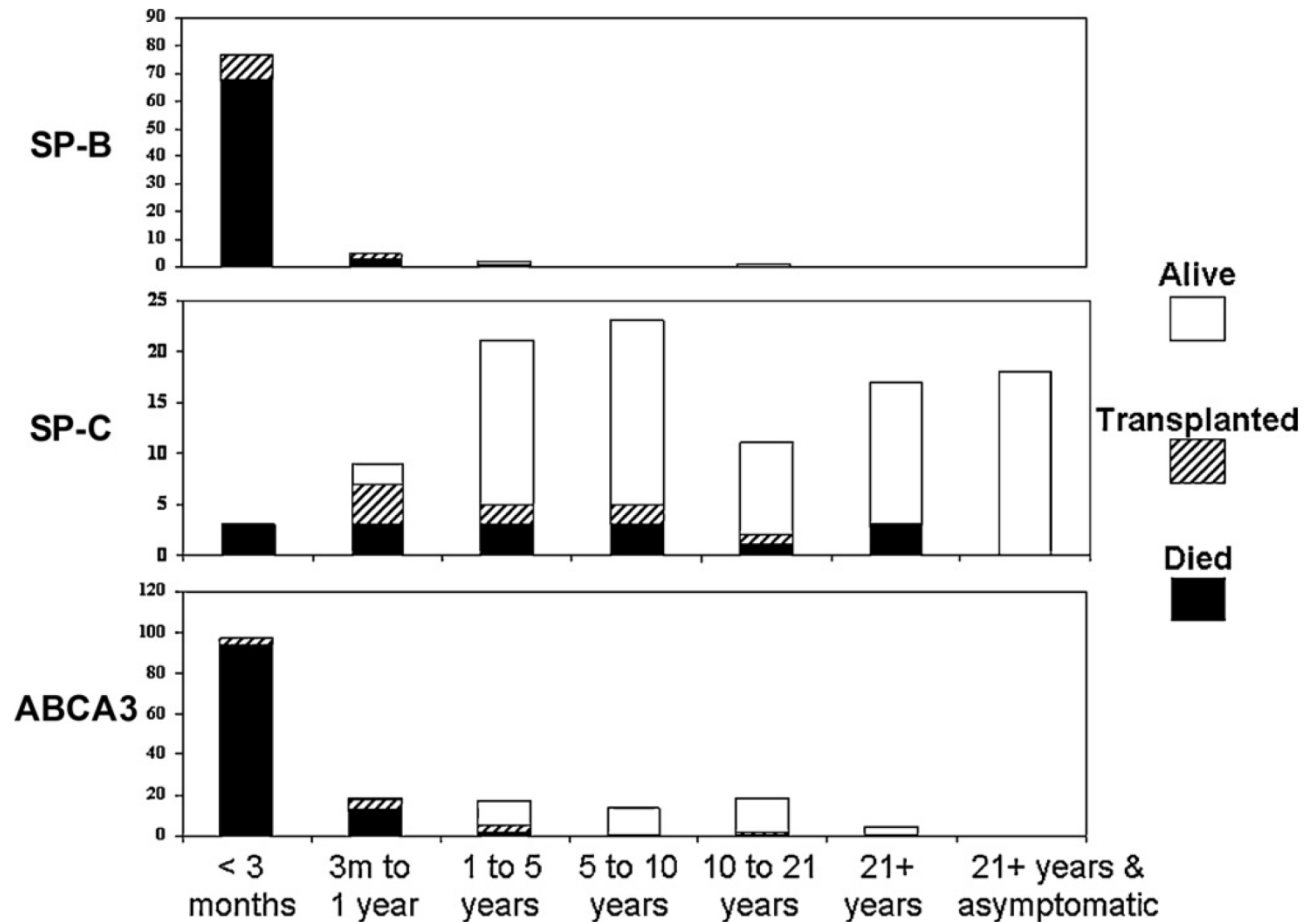
Abbreviations: AEC2, alveolar epithelial type 2 cells; AZM, azithromycin; CLD, chronic lung disease; F, female; HCQ, hydroxychloroquine; HRCT, high-resolution computerized tomography; ILD, interstitial lung disease; LB, lamellar bodies; LRTI, lower respiratory tract infection; M, male; m, month; MV, mechanical ventilation; MVB, multivesicular bodies; O₂, supplemental oxygen; PICU, pediatric intensive care unit; PL, phospholipids; PS, pulse steroids; PTX, pneumothorax; RDS, respiratory distress syndrome; w, weeks; y, years.

Genetic conditions causing surfactant protein dysfunction

	Protein function	Common genetic mutation	Inheritance pattern
SFTPB	Hydrophobic protein reduce surface tension	SP-B gene on chr 2, loss of gene function	Recessive
ABCA3	Transmembrane protein localised to surfactant- storing lamellar bodies for appropriate storage and release from AEC2	ABCA3 gene on chr 16 >150 mutations described	Recessive
SFTPC	Similar structure and function to SP-B	SP-C gene on chr 8	Dominant, variable penetrance usually spontaneous
NKX2.1	Transcription factor required for SP-B, SP-C and ABCA3 production	NKX2.1 gene on chr14 (encoding TTF1)	Dominant, usually spontaneous

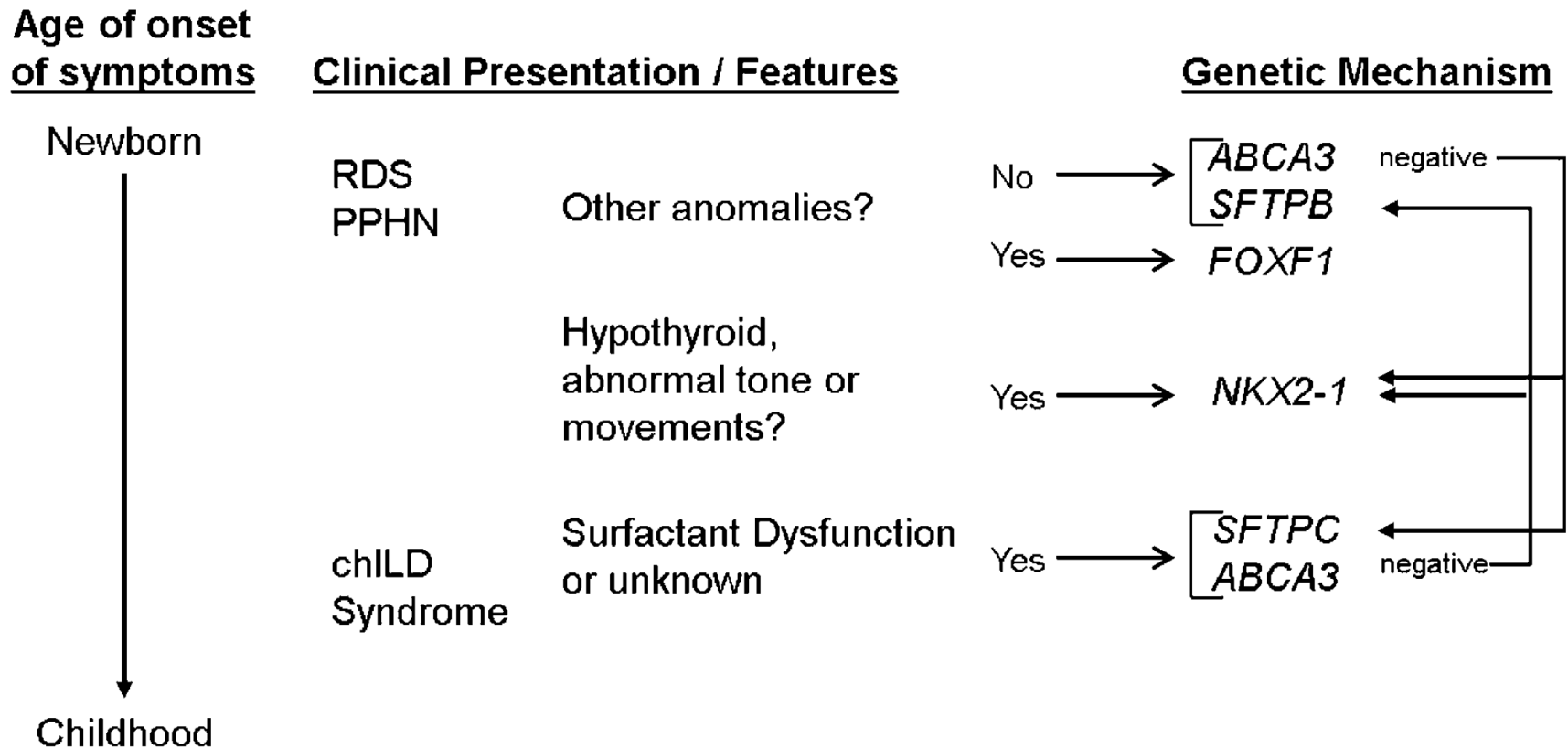
outcomes of patients with surfactant dysfunction disorders

Gower et al. Paediatric Respiratory Reviews 2011



numbers of patients who died (black filled), underwent lung transplantation (hatched), or were alive (open) by age ranges

Genetic approach to childhood interstitial lung disease (chILD) diagnosis



Neuroendocrine Cell Hyperplasia (NEHI)

Inheritance: sporadic, familial cases have been reported

Age of symptoms' onset: <1 yr of age

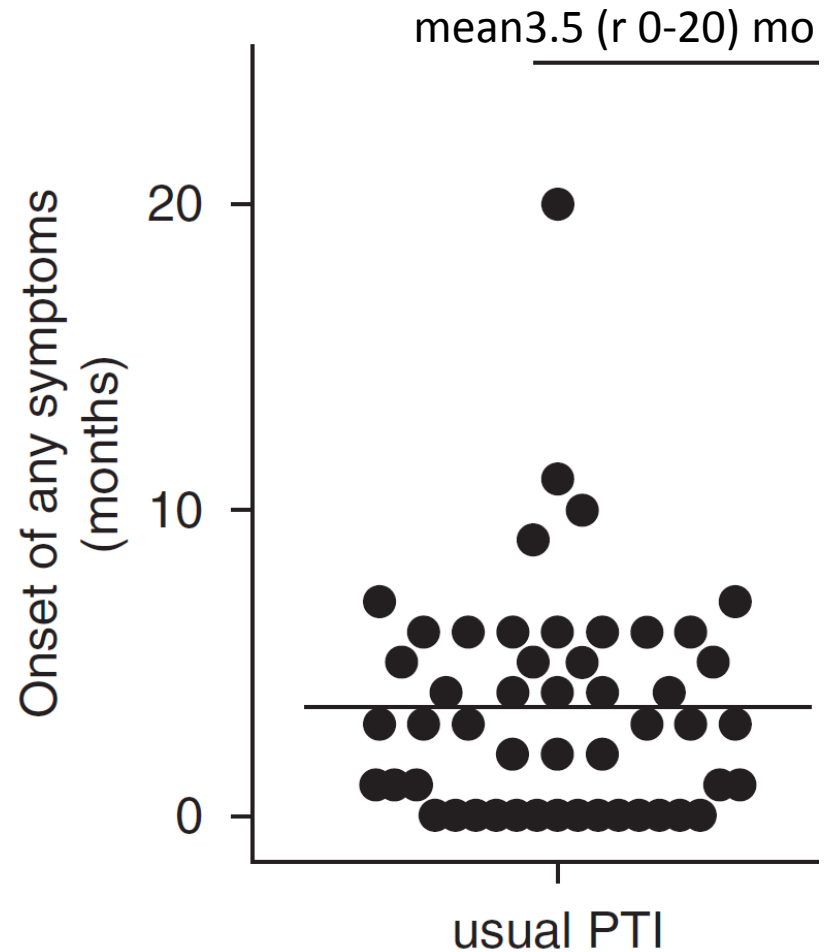
Clinical aspects: **tachypnea** with retractions, **crackles** and **hypoxemia** Failure to thrive

Histology: **normal histology** on standard staining, increased numbers of neuroendocrine cells on immunohistochemistry for bombesin

Persistent Tachypnea of Infancy (NEHI)

- retrospective cohort study
- 80 infants with PTI (NEHI)
- diagnosed on the basis of **clinical symptoms** and, if available, CT scans and lung biopsies.
- Oxygen supplementation - 60 (**75%**) infants

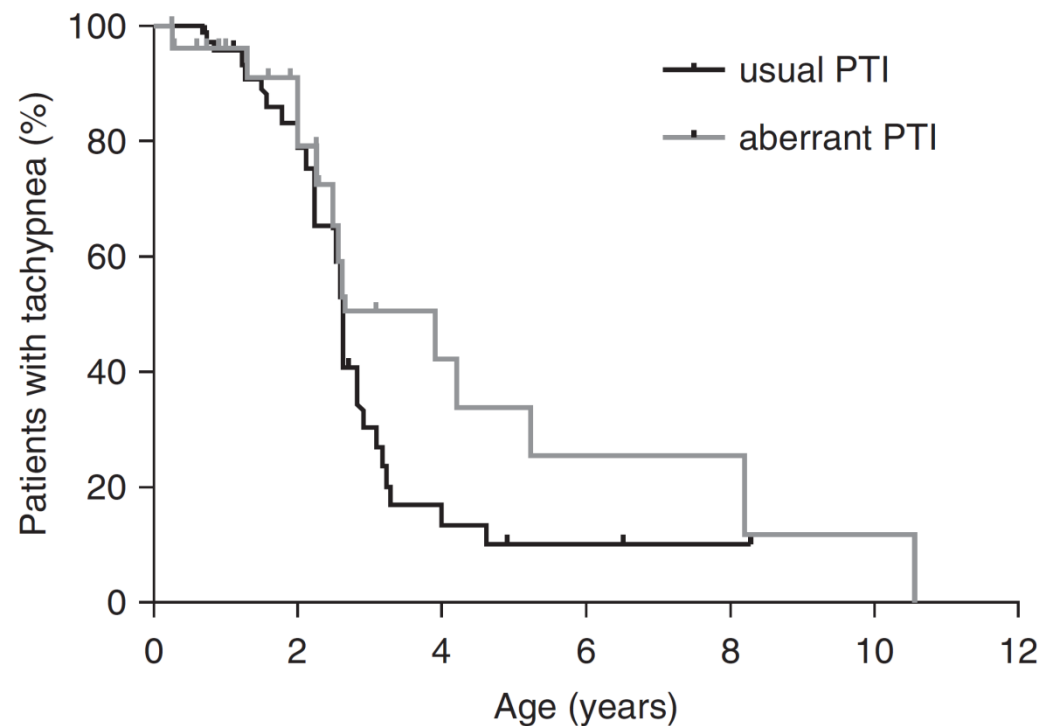
Rauch. Am J Respir Crit Care Med 2016



Persistent Tachypnea of Infancy (NEHI)

Duration of oxygen therapy
1.5 (0–5.3) yr

50% of all subjects had
overcome their tachypnea by
age 2.6 yrs



Persistent Tachypnea of Infancy (NEHI)

Rauch et al. Am J Respir Crit Care Med 2016
Cazzato et al. Early Hum Dev 2013

- PTI had a relatively **favorable prognosis**
- PTI can be diagnosed on the basis of **typical history** taking, clinical findings, and a **high-quality CT scan**.
- Further diagnostic measures, including lung **biopsies**, may be **limited to rare, complicated cases**.
- Treatment consists of **supplemental oxygen to prevent hypoxemia**



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Ancona, 21 ottobre 2017