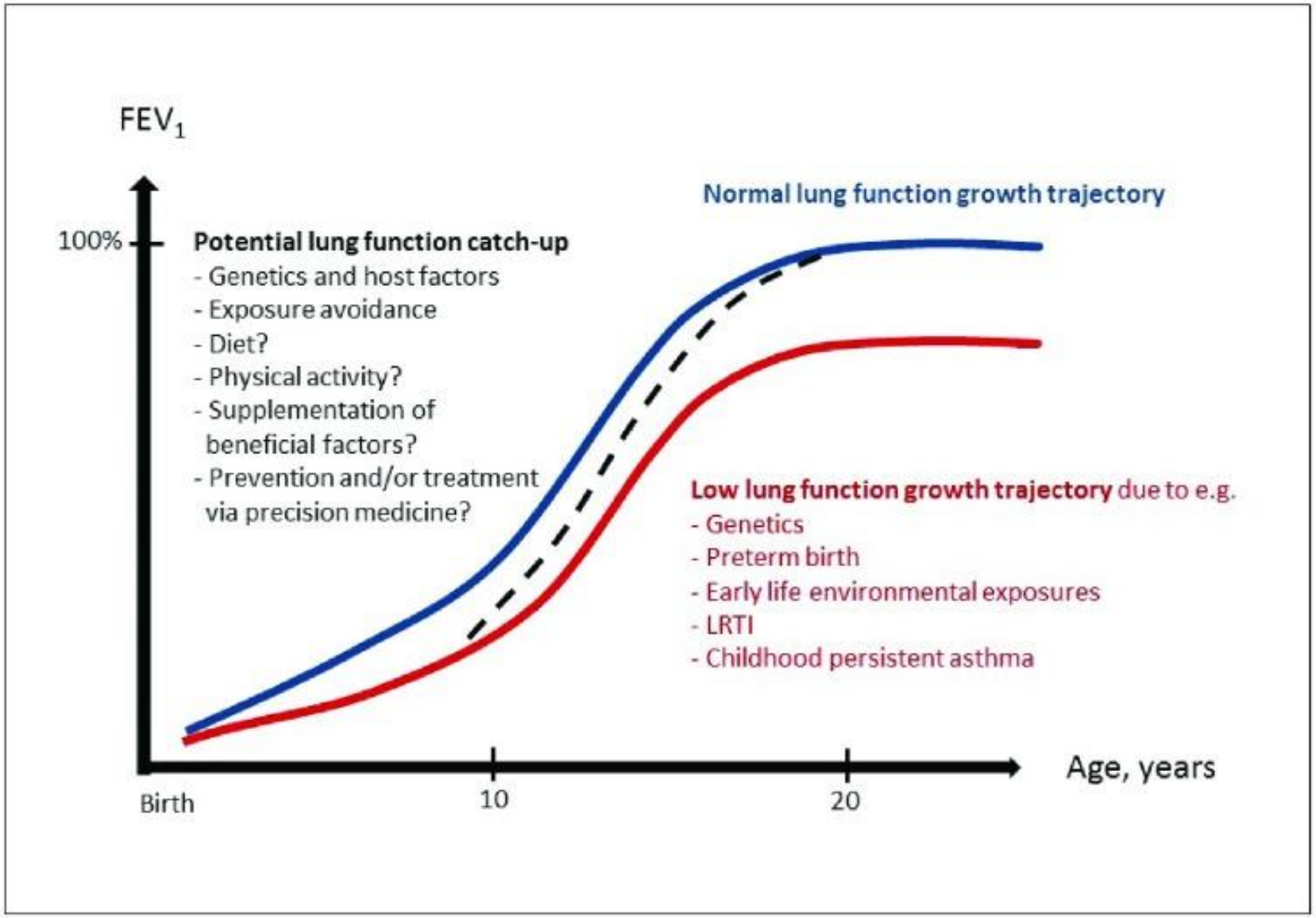
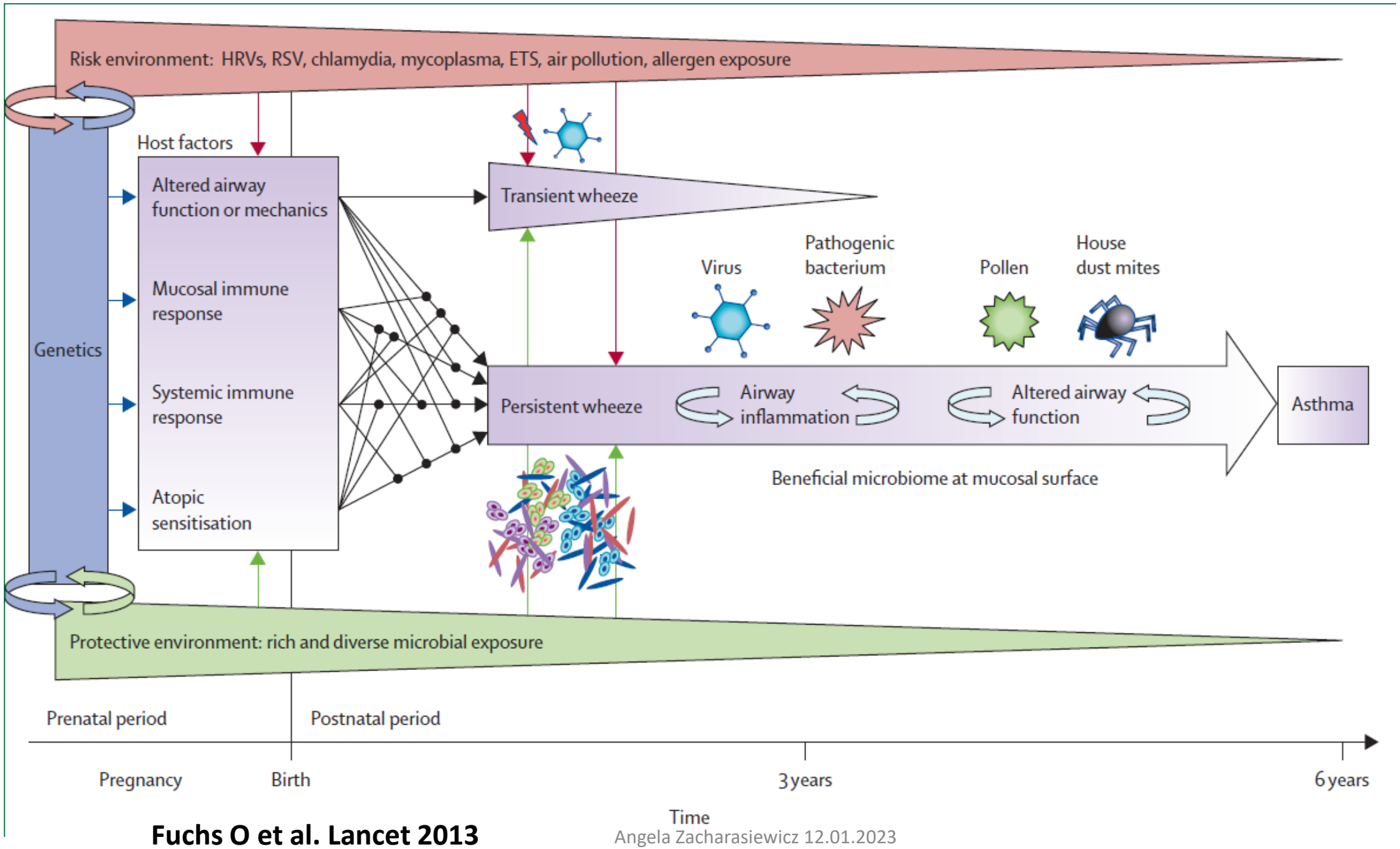
Neues aus der Pädiatrischen Pneumologie

Prof. Dr. Angela Zacharasiewicz

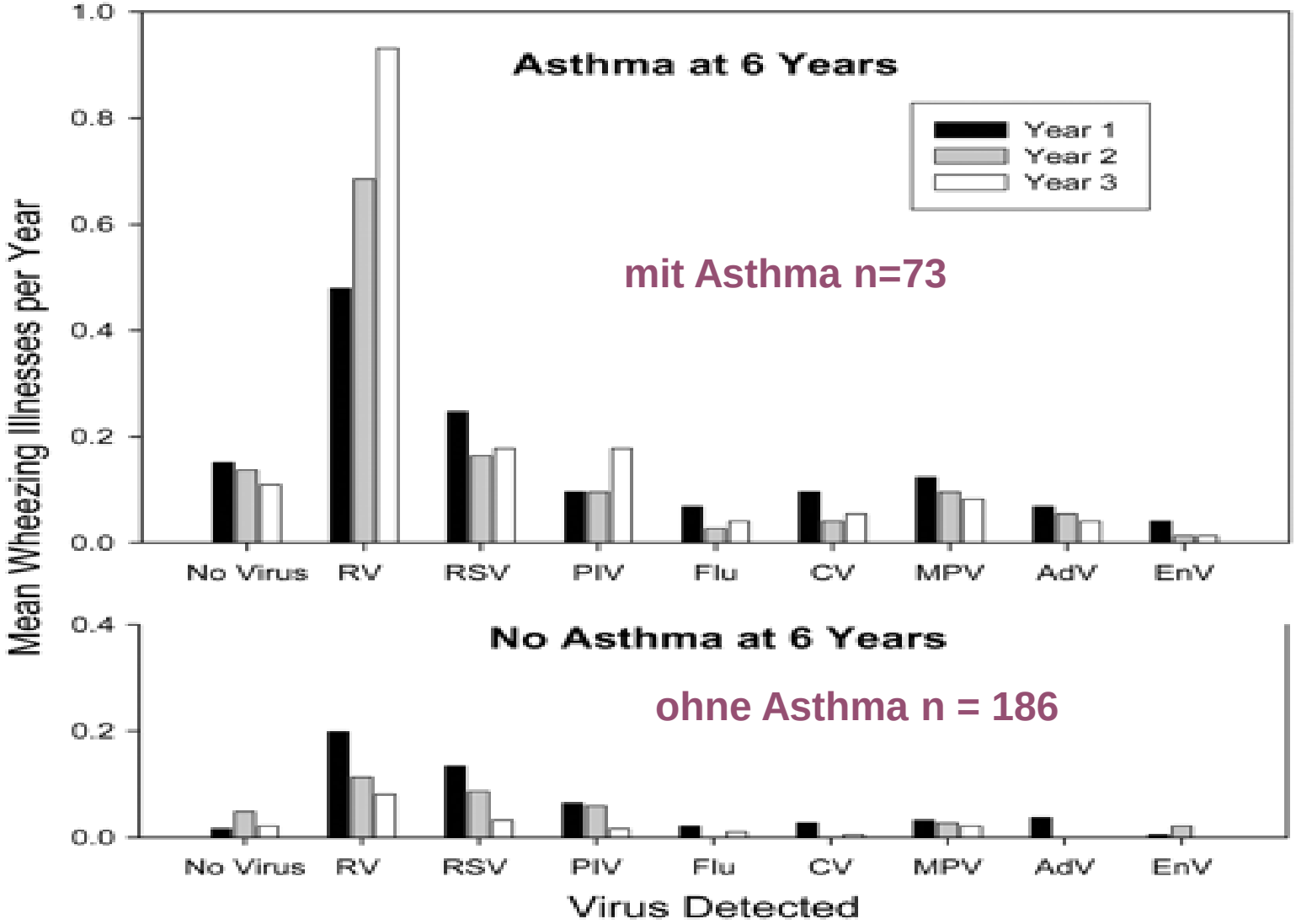


Erik Melén et al. F1000Res 2017

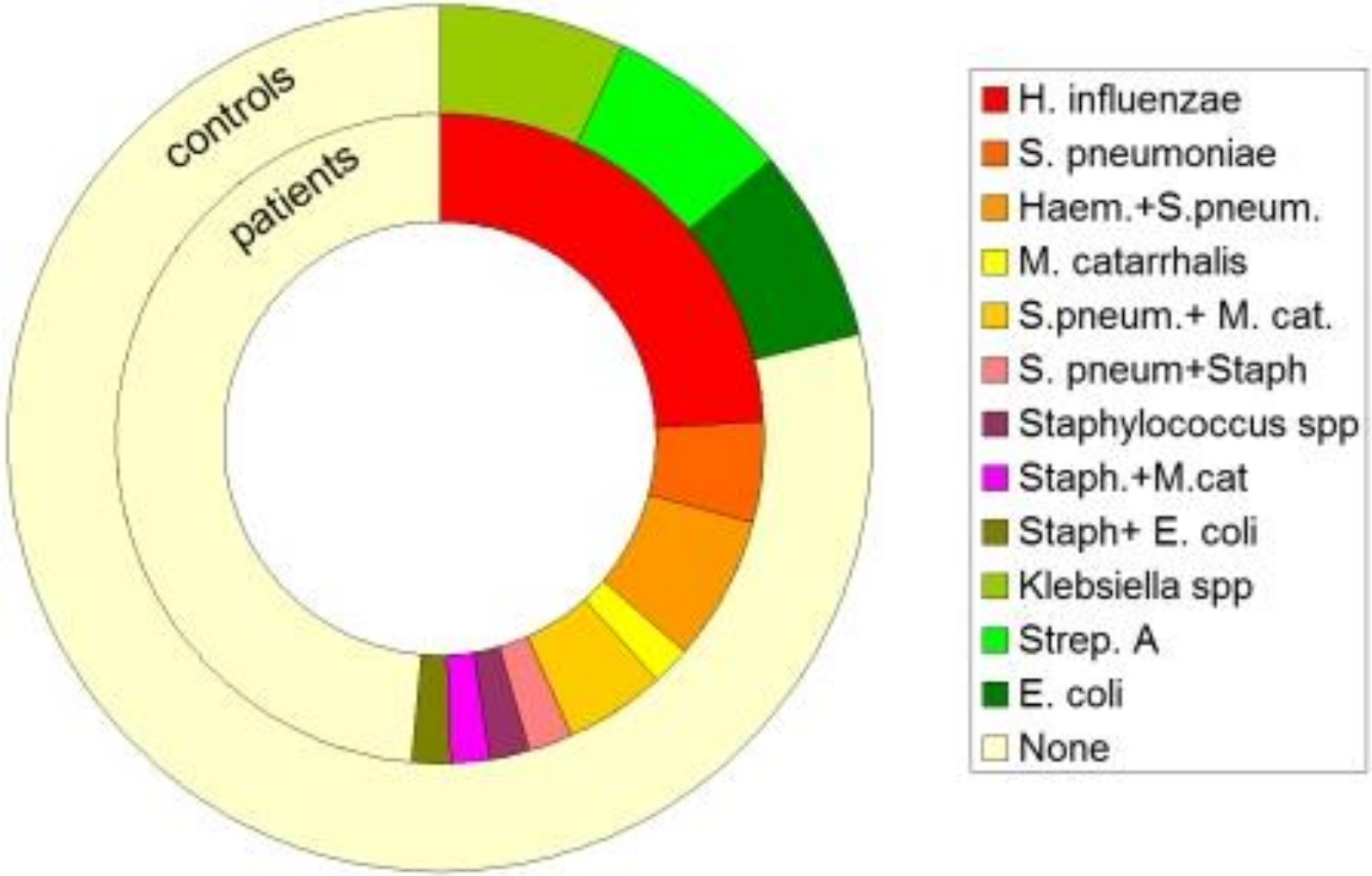


Fuchs O et al. Lancet 2013

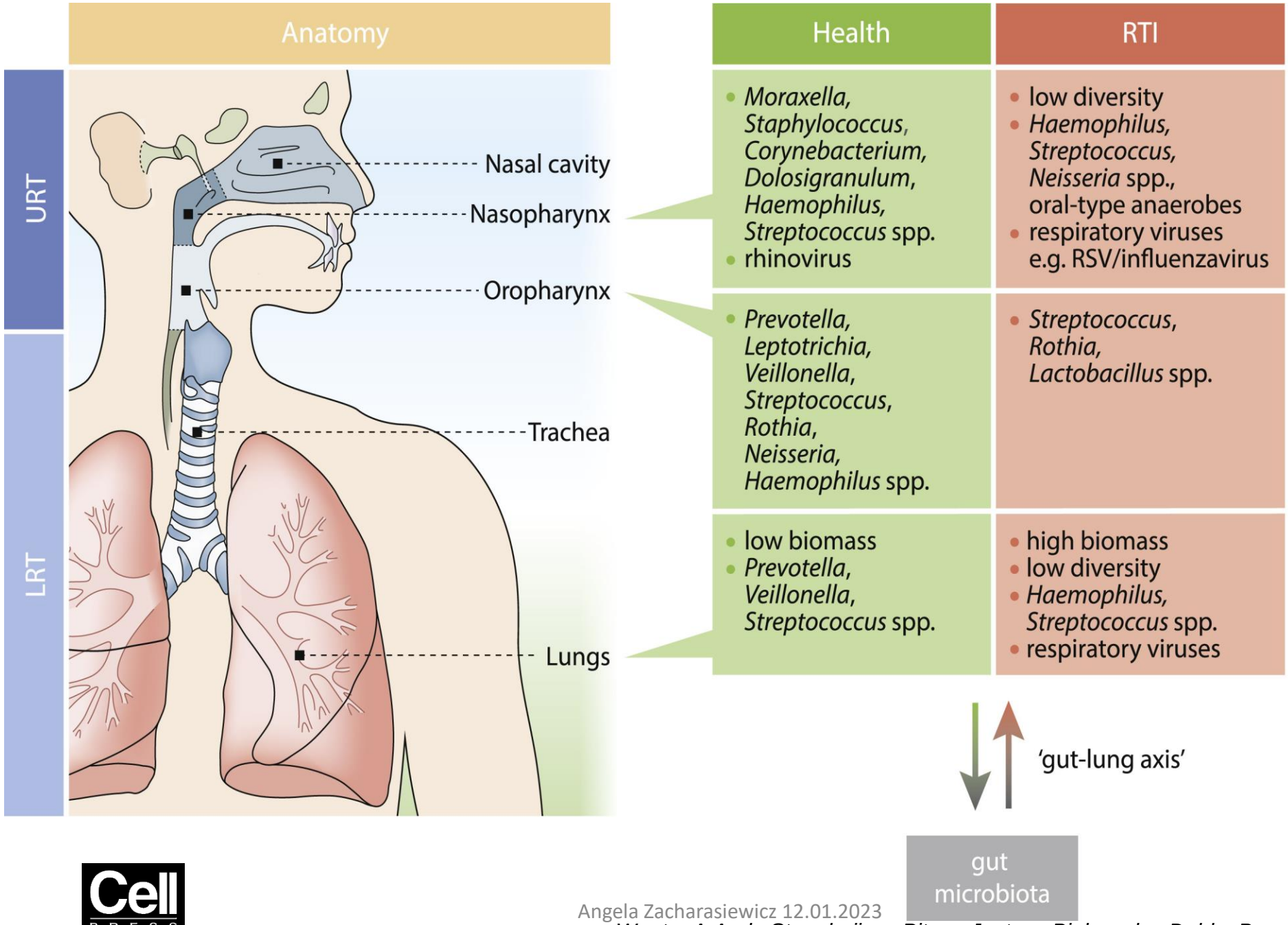
Which viruses cause wheeze in high risk infants?



Jackson et al. AJRCCM 2008; 178: 667–672.



Schwerk N et al. Plos One 2011



Wouter A.A. de Steenhuijsen Piters, Justyna Binkowska, Debby Bogaert Cell Host & Microbe 2020

- Palivizumab affects the spectrum of viral infections in infancy and prevents wheezing in early life

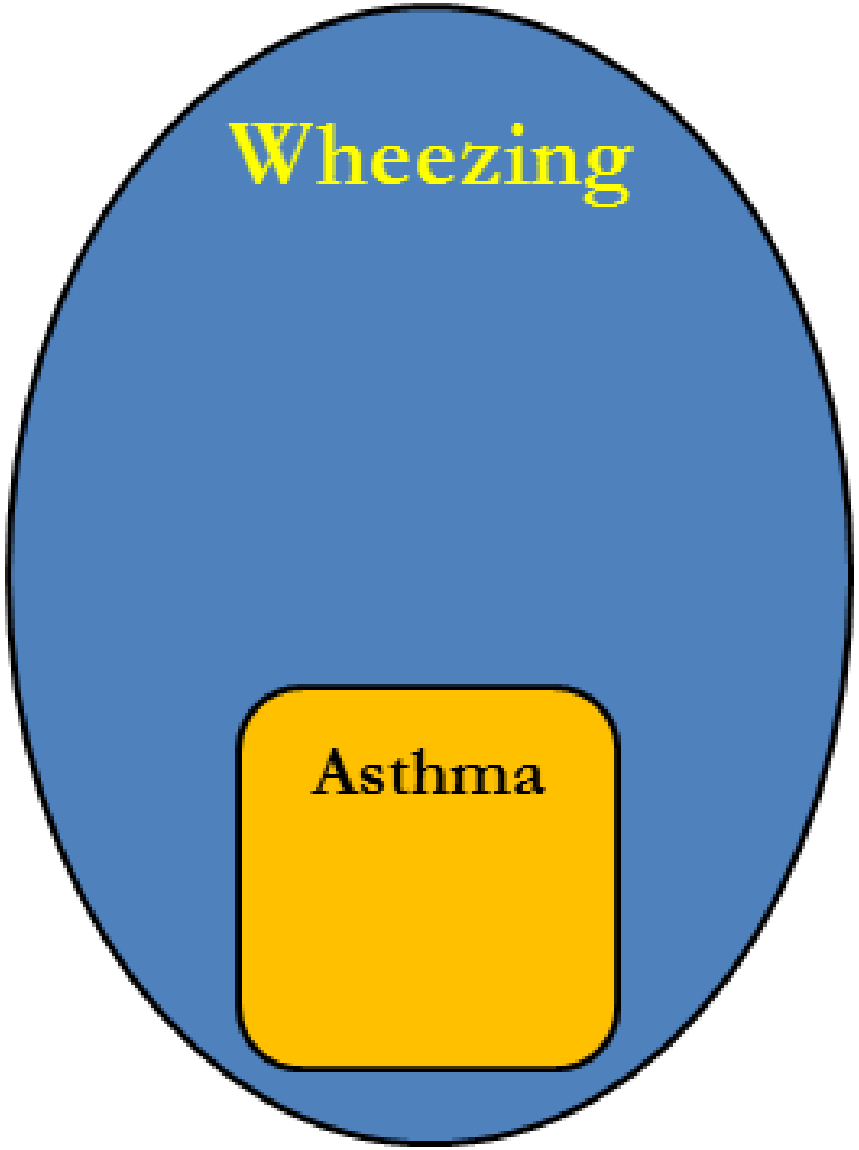
- However, in the long term, these effects seem to diminish, which might in part be explained by long-term ecological effects, including enrichment of more proinflammatory bacterial species, such as Haemophilus, and a reduction in potential beneficial species

Wing HM et al.

Lancet Respiratory 2020

Vitalparameter/Normwerteübersicht

Alter	**Neugeb.**	**6 Mon**	**1J**	**3J**	**5J**	**8J**	**12J**	**15J**
Gewicht (kg) (Jahre+4)x2	3,5	7	9	15	20	28	40	50
Herzfrequenz	140	120	110	105	105	95	95	80
RR	75/50	80/50	95/65	100/60	100/60	110/60	115/60	120/65
Atemfrequenz	40-50	30-40	20-30	20-30	16-20	16-20	14-16	14-16


Wheezing
Asthma

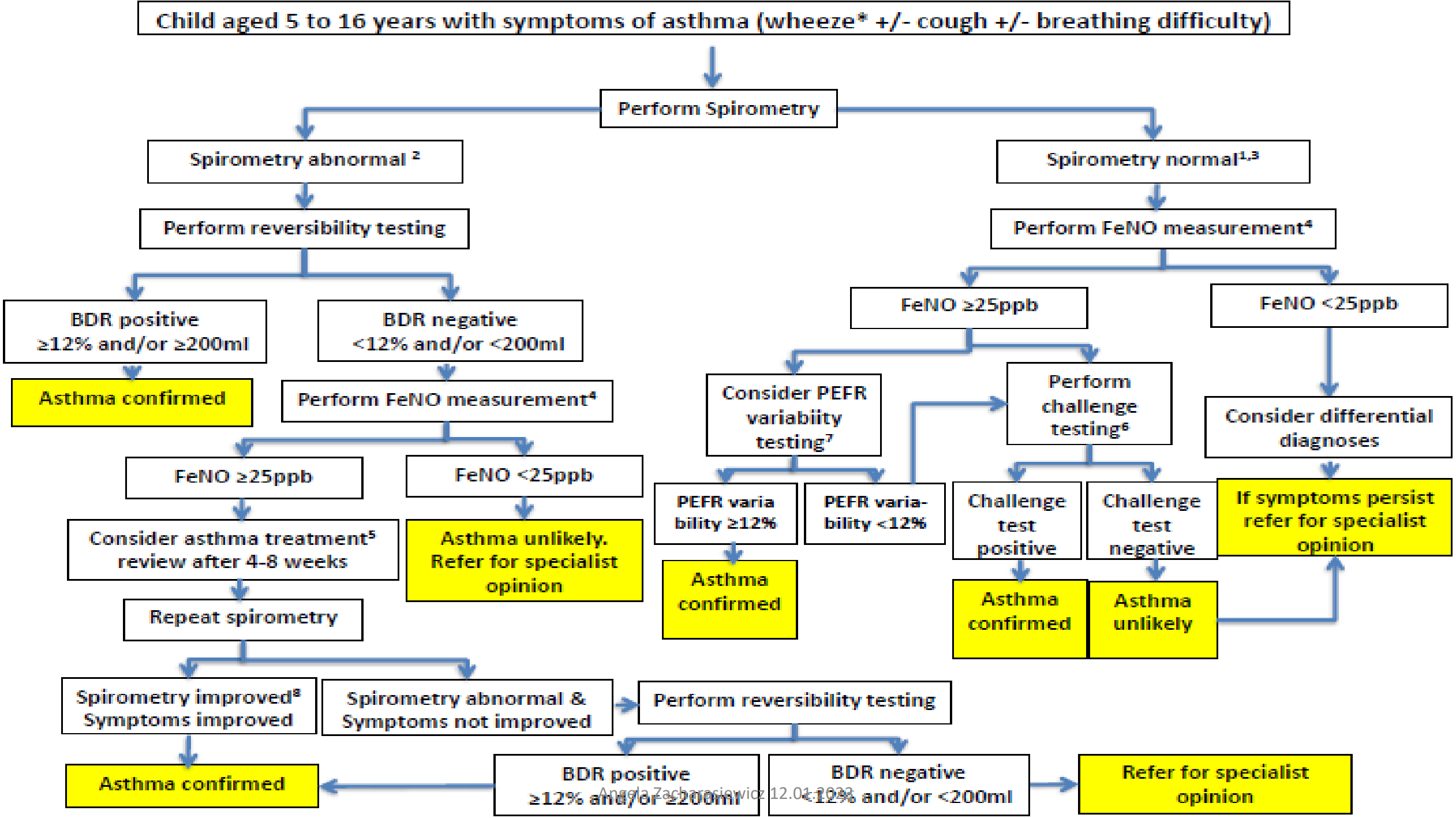
DIAGNOSE

EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
E.A. GAILLARD ET AL.

European Respiratory Society clinical practice guidelines for the diagnosis of asthma in children aged 5–16 years

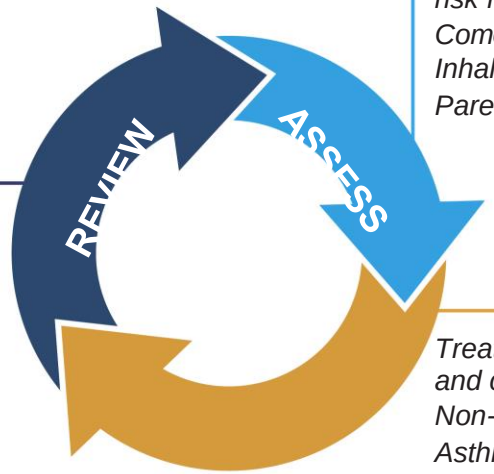
Erol A. Gaillard[1,2], Claudia E. Kuehni[3,4], Steve Turner[5], Myrofora Goutaki[3,4], Karl A. Holden[1], Carmen C.M. de Jong[3], Christiane Lex[6], David K.H. Lo[1,2], Jane S. Lucas[7,8], Fabio Midulla[9], Rebeca Mozun[3], Giorgio Piacentini[10], David Rigau[11], Bart Rottier[12,13,14], Mike Thomas[15], Thomy Tonia[3], Jakob Usemann[16,17], Ozge Yilmaz[18], Angela Zacharasiewicz[19] and Alexander Moeller[17]

[1]Dept of Respiratory Sciences, Leicester NIHR Biomedical Research Centre (Respiratory theme), University of Leicester, Leicester, UK. [2]Dept of Paediatric Respiratory Medicine, Leicester Children's Hospital, University Hospitals Leicester, Leicester, UK. [3]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland. [4]Paediatric Respiratory Medicine, Children's University Children's Hospital, University of Bern, Bern, Switzerland. [5]Child Health, University of Aberdeen, Aberdeen, UK. [6]Dept of Paediatric Cardiology, Intensive Care Medicine and Neonatology with Paediatric Pulmonology, University Medical Center Goettingen, Goettingen, Germany. [7]Primary Ciliary Dyskinesia Centre, National Institute for Health Research, Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK. [8]University of Southampton Faculty of Medicine, School of Clinical



Children 5 years and younger

Personalized asthma management:
Assess, Adjust, Review response



Exclude alternative diagnoses
Symptom control & modifiable risk factors
Comorbidities
Inhaler technique & adherence
Parent preferences and goals

Symptoms
Exacerbations
Side-effects
Parent satisfaction

Treat modifiable risk factors and comorbidities
Non-pharmacological strategies
Asthma medications
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4
PREFERRED CONTROLLER CHOICE		Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for pre-school children)	Double 'low dose' ICS	Continue controller & refer for specialist assessment
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider intermittent short course ICS at onset of viral illness*	*Daily leukotriene receptor antagonist (LTRA), or intermittent short course of ICS at onset of respiratory illness*	*Low dose ICS + LTRA Consider specialist referral*	*Add LTRA, or increase ICS frequency, or add intermittent ICS*
RELIEVER	As-needed short-acting beta$_2$-agonist			
CONSIDER THIS STEP FOR CHILDREN WITH:	Infrequent viral wheezing and no or few interval symptoms	Symptom pattern not consistent with asthma but wheezing episodes requiring SABA occur frequently, e.g. ≥3 per year. Give diagnostic trial for 3 months. Consider specialist referral.	Asthma diagnosis, and asthma not well-controlled on low dose ICS	Asthma not well-controlled on double ICS
		Symptom pattern consistent with asthma, and asthma symptoms not well-controlled or ≥3 exacerbations per year.	Before stepping up, check for alternative diagnosis, check inhaler skills, review adherence and exposures	

Angela Zacharasiewicz 12.01.2023

Asthma-Kontrolle

Kriterium (letzten 4 Wochen)*	Kontrolliertes Asthma (alle Kriterien erfüllt)	Teilweise kontrolliertes Asthma (1 bis 2 Kriterien innheralb 1 Woche)	Unkontrolliertes Asthma
Symptome tagsüber	< 2x pro Woche nein#	> 2x pro Woche ja#	Drei oder mehr Kriterien des "teilweise kontrollierten Asthma" innerhalb einer Woche erfüllt
Einschränkungen von Aktivitäten im Alltag	nein	ja	
Nächtliche/s Symptome/Erwachen	nein	ja	
Einsatz einer Bedarfsmedikation/ Notfallbehandlung	< 2x pro Woche nein#	> 2x pro Woche ja#	
Lungenfunktion (PEF oder FEV1)	normal	< 80 % des Sollwertes (FEV1) oder oder des persönlichen Bestwertes (PEF)	
Exazerbation†	nein	ein oder mehrere pro Jahr	eine pro Woche

*** bei KINDERN: KEINE SYMPTOME, KEINE BEDARFSMEDIKATION!**

Apropos Lungenfunktion:
Wie messe ich den Therapieeffekt?

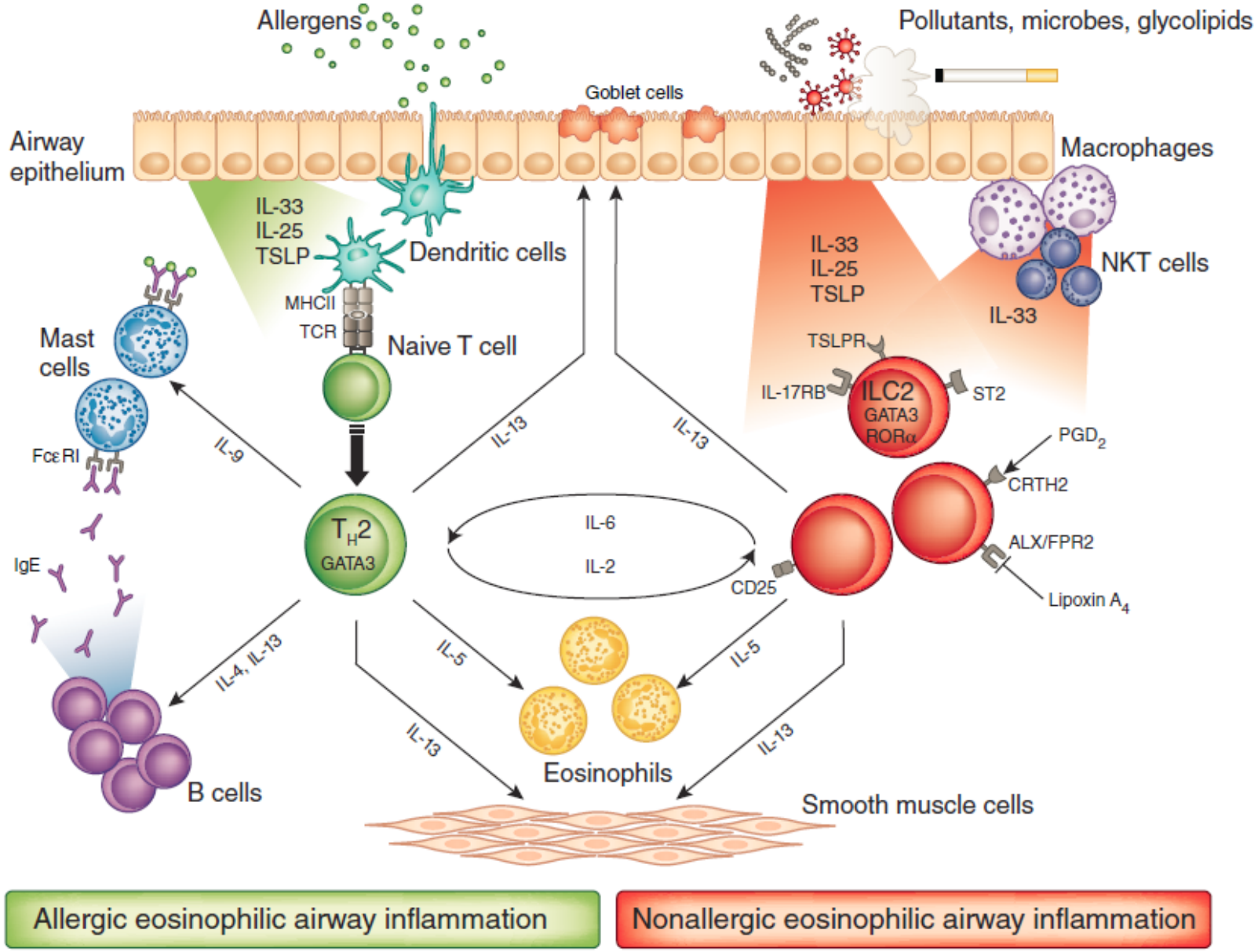
- Die meisten Schulkinder haben eine normale Lungenfunktion unabhängig vom Asthma Schweregrad

- Asthma Schweregrad korreliert nicht mit FEV_1

- Isolierte Lungenfunktionswerte sind nicht zuverlässig

  → mehrfache Messungen nötig

Bacharier LB et al. Am J Respir Crit Care Med 2004; 170: 426-432



ILC2: Type 2 innate lymphoid cells

Brusselle GG, et al. *Nature Med* 2013

Montelukast

- March 2020 Boxed Warnung FDA
  - strongest form of warning of the FDA
  - when medical studies suggest that taking a medication is associated with severe or life threatening side effects

- Recommendation:
  - For asthma: careful consideration of risk benefits ratio
  - Immediate discontinuation of montelukast and consultation with doctor, if such side effects occur

Box 2: Neuropsychiatric reactions associated with montelukast[7 8]

Uncommon (≥1/1000 to <1/100)

- Agitation, including aggressive behaviour or hostility
- Sleep disturbances such as trouble sleeping, bad or vivid dream sleepwalking
- Depression
- Feeling anxious
- Restlessness or irritability

BMJ 2022;376:e067554

Rare (≥1/10 000 to <1/1000)

- Memory problems
- Attention problems
- Tremor or shakiness, uncontrolled muscle movements

Very rare (<1/10 000)

- Obsessive-compulsive symptoms
- Hallucinations
- Stammering
- Suicidal thoughts and actions (including suicide)
- Disorientation or confusion

Biologika

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5 Anti-IL5R	Mepolizumab (SC) Reslizumab (IV) Benralizumab (SC)	≥6 years ≥18 years ≥12 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
Anti-IL4R	Dupilumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥12 years	Severe asthma	

Diagnosis and Management of Difficult-to-treat & Severe Asthma [Internet]. Global Initiative for Asthma - GINA. [zitiert 9. November 2022]. Verfügbar unter: https://ginasthma.org/severeasthma/

Conclusio schweres Asthma

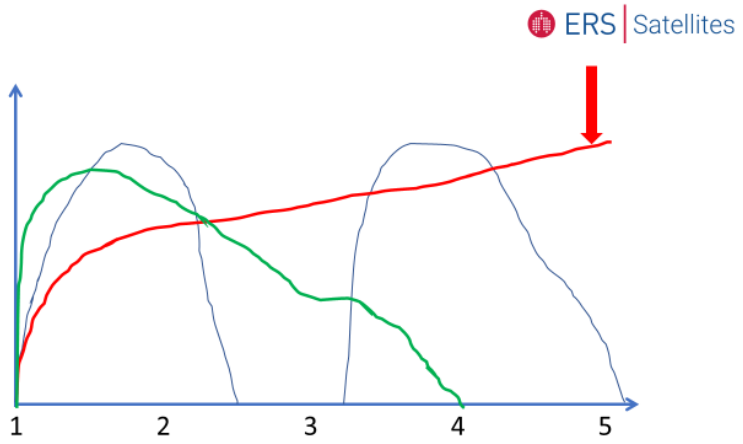
- Problematic severe asthma: Difficult to treat oder treatment resistant
- Engmaschiges Monitoring
- Nächtliche Beschwerden

- Schlechte Übereinstimmung zwischen subjektiver Einschätzung objektiver Messung
- Cave: persistierend erhöhtes FeNO und Lungenfunktionsverschlechterung
- Keine OCS!
- Keine Angst vor Biologika - bitte überweisen Sie an Pädiatrische Pneumologie zur Evaluierung und Ersteinstellung

Wichtige Fragen:

- How did the coughing start?
- Since when is your child coughing?
- Tendency?
- Triggers?
- Wet or dry cough?
- Other characteristics?
- Other symptoms?

Timing, Tendency, Triggers	3 x T
Sound, Signs, other Symptoms	3 x S



Shields et al. BTS Guidelines Thorax 2007

Cave:

Cortical control

Different perception

Red flags für chronische und/oder schwere Erkrankung

timing:
- Start bei Geburt
- Plötzlicher Beginn
- persistierend
- Immer bei Nahrungsaufnahme

tendency:
- Schlechter werdend
- feuchter Husten

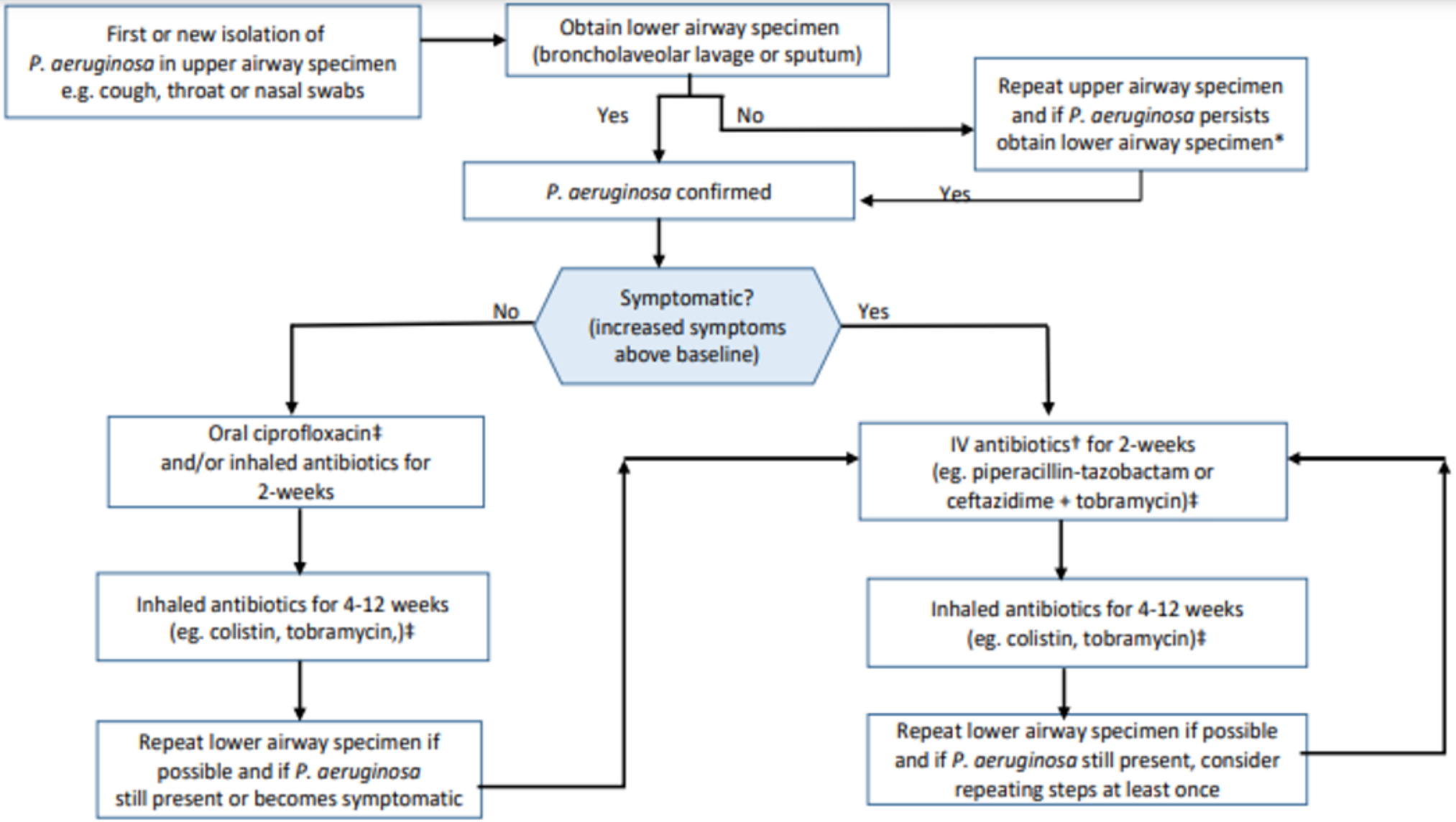
Zusätzliche Symptome:
- failure to thrive
- Gewichtsverlust
- Fieber, Nachtschweiss
- Andere Symptome
- Pathologische Auskultation
- Hypoxie, thorakale Schmerzen
- Dyspnoe in Ruhe /bei Belastung
- Abnormes Geräusch beim Husten
- Neurologische Störungen/Entwicklungsverzögerung etc.

Non-CF Bronchiektasien: Phänotypische Präsentation

- Chronischer produktiver Husten>4 Wochen, auch zwischen Virusinfekten
- Produktiver Husten mit manchmal purulentem Sputum bei älteren Kindern (morgens)
- Persistierender Husten und pathologische Auskultation
- Persistierender Husten trotz prolongierter Antibiose
- Unvöllständige Resolution einer Pneumonie oder wiederholte Pneumonien
- Unerklärte Hämoptysen
- Asthma-ähnliche Symptome, die nicht auf Therapie ansprechen
- Dyspnoe, Müdigkeit, Uhrglasnägel, Thoraxdeformitäten, schlechte Gewichtszunahme

CF, cystic fibrosis.

Kantar A. J Thorac Dis 2017; 9(4): 907–13.



* If lower airway specimen unobtainable, no treatment if asymptomatic; treat with intravenous anti-pseudomonal antibiotics for 2-weeks if symptomatic;
†Although there is no trial evidence, many paediatricians would employ a two-drug combination of intravenous antibiotics. The recommendation for administering two antibiotics when employing short (2-week) IV antibiotic courses aligns with the studies included in the systematic review and the ERS adult guidelines;
‡Antibiotics choices are dependent upon patient factors (e.g. adherence, tolerance, preference), availability of antibiotics and *P. aeruginosa* susceptibility profile.

Figure 3

Suggested management approach used by the panel when *Pseudomonas aeruginosa* is first or newly-isolated in a child with bronchiectasis. The

improvebe.org

Children's Bronchiectasis Education, Advocacy and Research Network

ne About Who we are Learning from families Publications News & Resources Members Support Registry Contact

European Respiratory Society guidelines for the management of children and adolescents with bronchiectasis

Anne B. Chang[1,2], Rebecca Fortescue[3], Keith Grimwood[4,5], Efthymia Alexopoulou[6], Leanne Bell[7], Jeanette Boyd[8], Andrew Bush[9], James D. Chalmers[10], Adam T. Hill[11], Bulent Karadag[12], Fabio Midulla[13], Gabrielle B. McCallum[2], Zena Powell[7], Deborah Snijders[14], Woo-Jung Song[15], Thomy Tonia[16], Christine Wilson[17], Angela Zacharasiewicz[18] and Ahmad Kantar[19]

[1]Dept of Respiratory and Sleep Medicine, Queensland Children's Hospital and Australian Centre for Health Services Innovation, Queensland University of Technology, Brisbane, Australia. [2]Child Health Division, Menzies School of Health Research, Darwin, Australia. [3]Population Health Research Institute, St George's University of London, London, UK. [4]Depts of Infectious Disease and Paediatrics, Gold Coast Health, Southport, Australia. [5]School of Medicine and Menzies Health Institute Queensland, Griffith University, Southport, Australia. [6]2nd Radiology Dept, National and Kapodistrian University of Athens, Attikon University Hospital, Athens, Greece. [7]Bronchiectasis Paediatric Patient Advisory Group, European Lung Foundation, Alnwick, UK. [8]European Lung Foundation, Sheffield, UK. [9]Dept of Paediatric Respiratory Medicine, Royal Brompton Hospital and National Heart and Lung Institute, School of Medicine, Imperial College London, London, UK. [10]College of Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee, UK. [11]Dept of Respiratory Medicine, Royal Infirmary and University of Edinburgh, Edinburgh, UK. [12]Division of Pediatric Pulmonology, Faculty of Medicine, Marmara University, Istanbul, Turkey. [13]Dept of Maternal Science, Sapienza University of Rome, Rome, Italy. [14]Dipartimento Salute della Donna e del Bambino, Università degli Studi di Padova, Padova, Italy. [15]Dept of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. [16]Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland. [17]Dept of Physiotherapy, Queensland Children's Hospital, Brisbane, Australia. [18]Dept of Pediatrics and Adolescent Medicine, Teaching Hospital of the University of Vienna, Wilhelminen Hospital, Klinikum Ottakring Vienna, Wien, Austria. [19]Pediatric Asthma and Cough Centre, Istituti Ospedalieri Bergamaschi, University and Research Hospitals, Ponte San Pietro, Italy.

Corresponding author: Anne B. Chang (Anne.chang@menzies.edu.au)

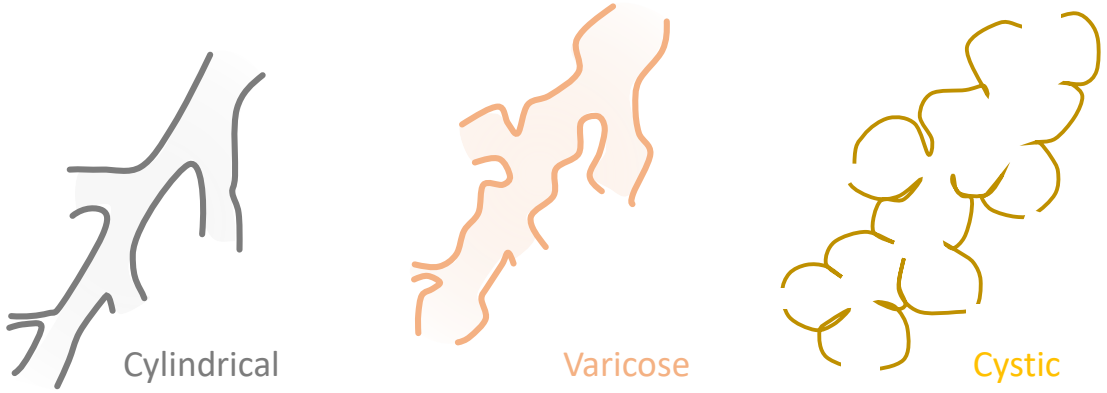
Angela Zacharasiewicz 12.01.2023

Shareable abstract (@ERSpublications)

Definition von Bronchiektasien

Severe bronchiectasis:

Increasing BAR	Distinct morphological appearance



Other non-pathognomonic CT features are:

Bronchial wall thickening

Lack of bronchial tapering [from central to periphery]

Bronchial structures present in the lung periphery

Mucus plugs

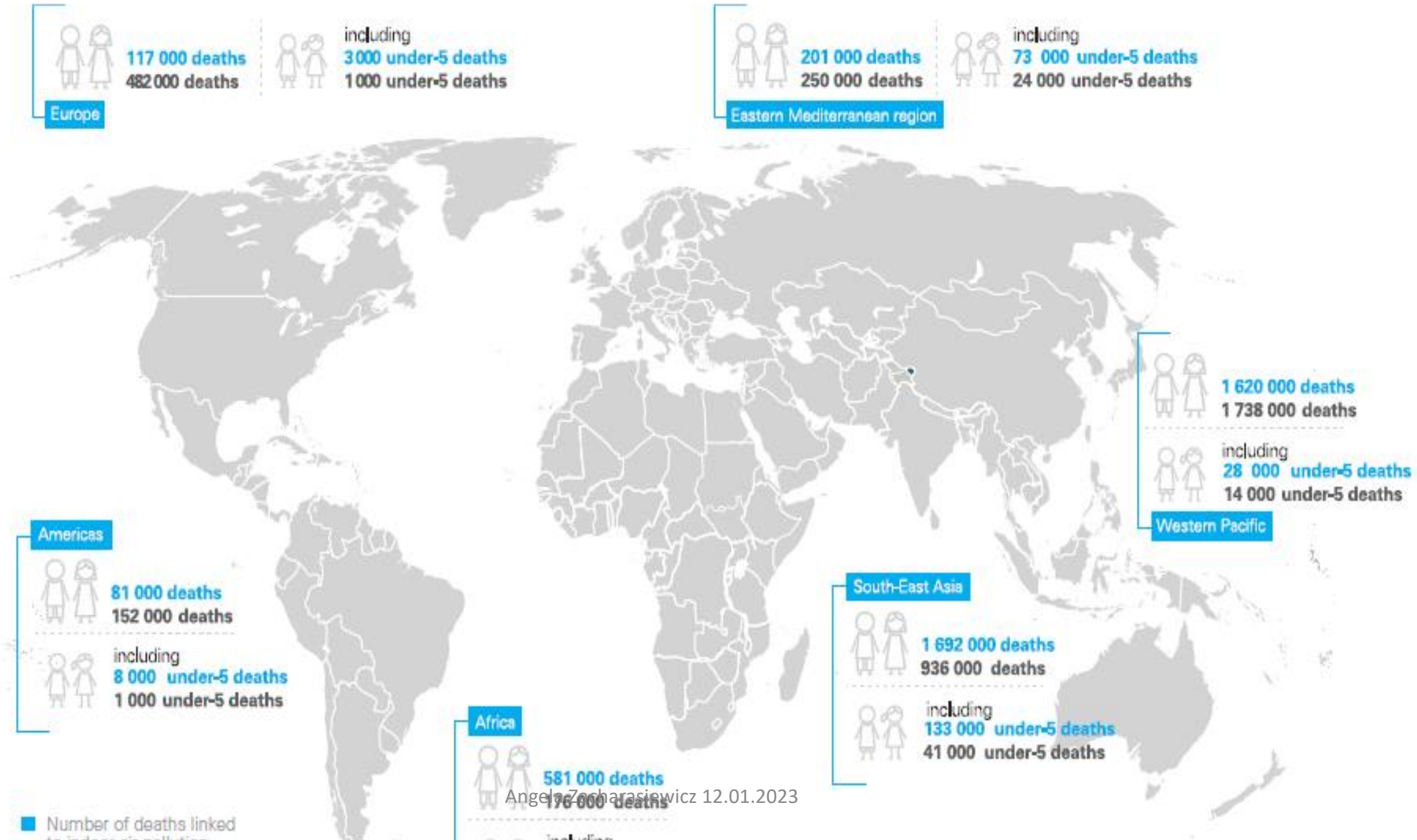
Mosaic perfusion reflecting air-trapping

BAR, broncho-arterial ratio.

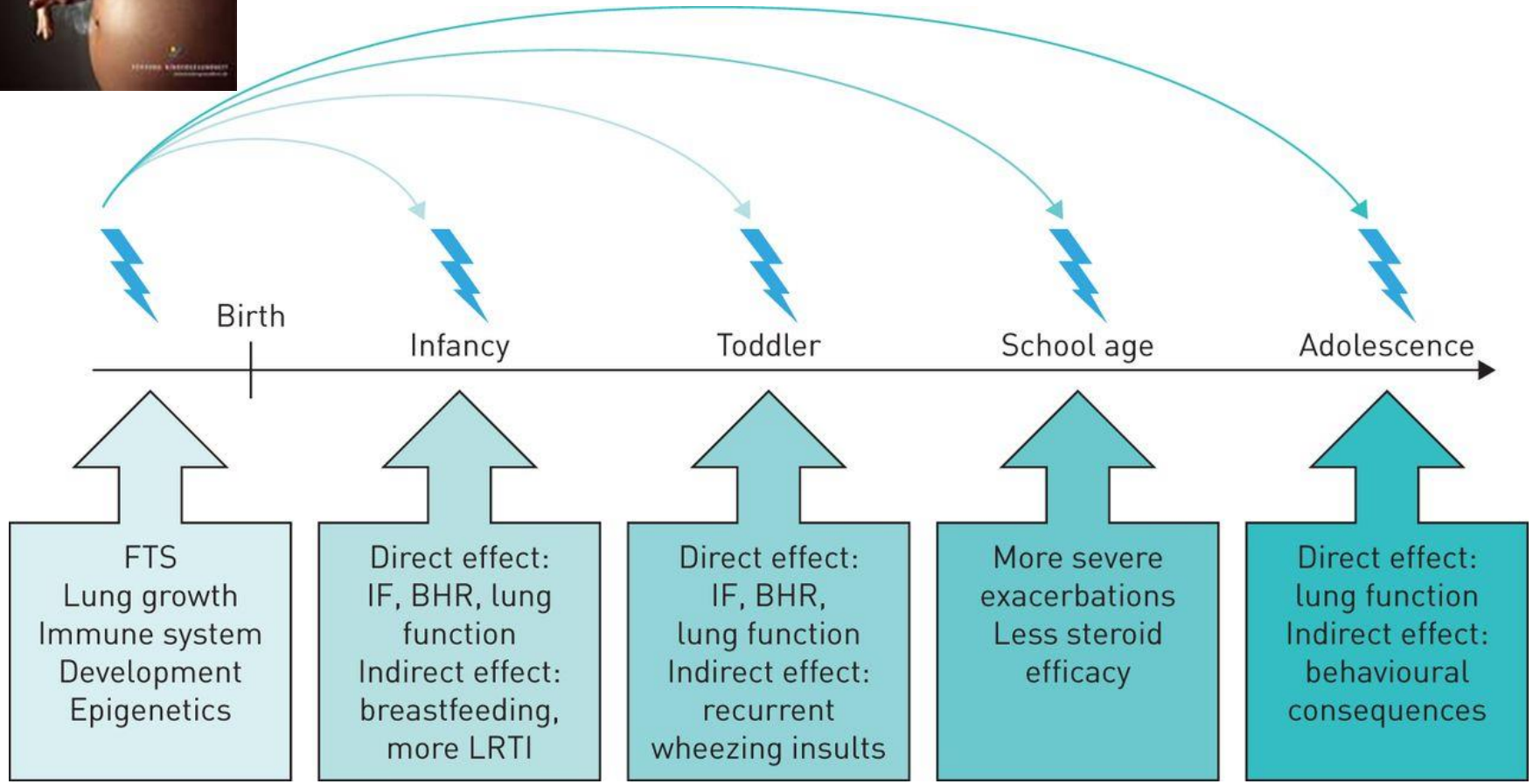
Chang AB, et al. Manuscript under review.

Nearly 1 in 10 under-5 deaths is linked to air pollution

Fig. 7: Regional breakdown of deaths from outdoor and indoor air pollution, 2012



Summary of effects of maternal smoking in pregnancy (MSP) on asthma from infancy to adolescence



Angela Zacharasiewicz ERJ Open Res 2016;2:00042-2016