Astma in het jonge kind

Dr. J. Willekens

Kinderlongziekten UZ Gent

Overzicht

- Definitie
- Prevalentie
- Pathogenese
- Prognose
- Diagnose
- Behandeling

Definitie astma

- Herhaalde episoden van hoesten, wheezing, kortademigheid
- Variatie in tijd, frequentie en intensiteit
- Chronische luchtweginflammatie
- Reversibele luchtwegobstructie

GINA guidelines 2018

Astma in kind <5 jaar

Preschool wheezing

Viral induced wheezing

Happy wheezer

Zuigelingenastma

Recidiverende bronchiolitis

Bronchiale hyperreactiviteit

- Reversibele obstructie?
- Luchtweginflammatie?

Not all that wheezes is asthma

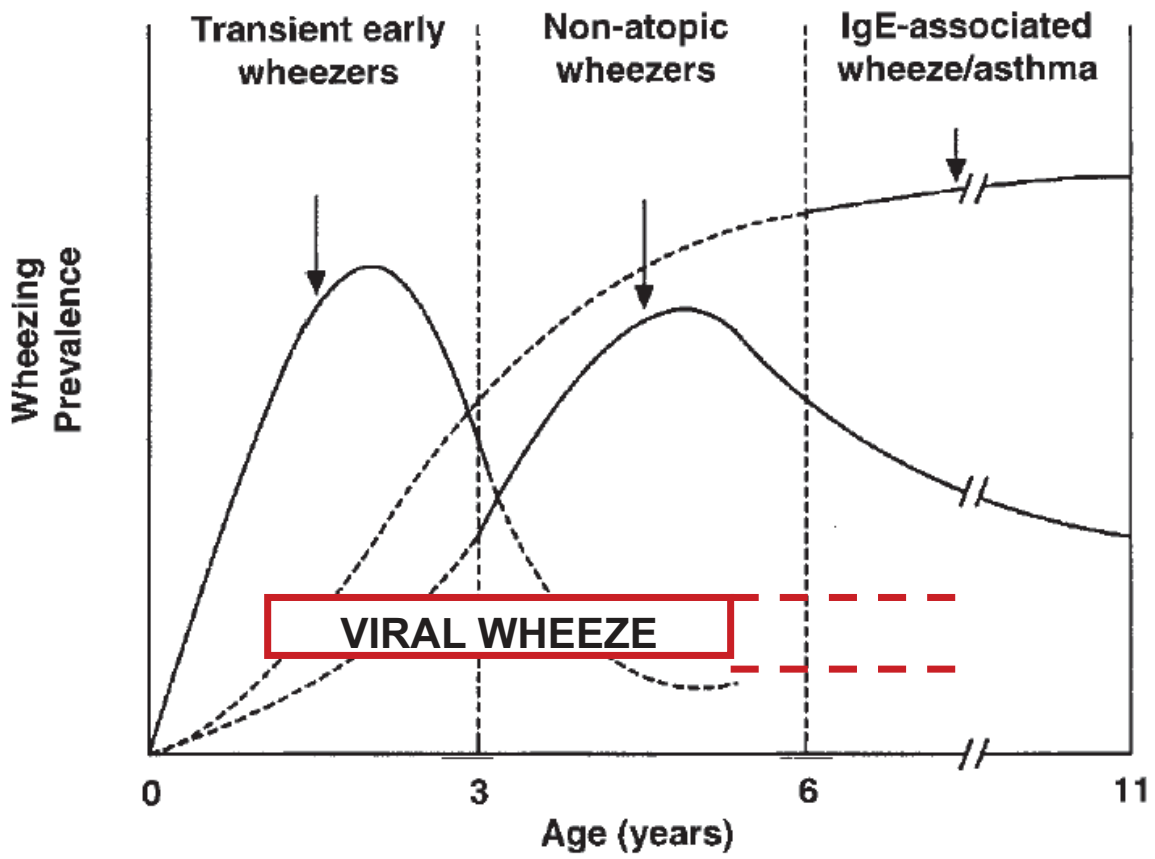
- Moeilijke diagnose!

- Frequent wheezing in jonge kinderen met luchtweginfectie
  - Velen zullen geen astma ontwikkelen
  - Astma medicatie kan geïndiceerd zijn onafhankelijk van diagnose van astma

Wheezing

- Parent-reported vs. physician-observed
- Piepende ademhaling agv. vernauwing thv. onderste luchtwegen
- Differentiëren met andere respiratoire geluiden
  - Inspiratoir vs. expiratoir
  - Reutelen, stridor, ronchi…

Preschool asthma phenotypes

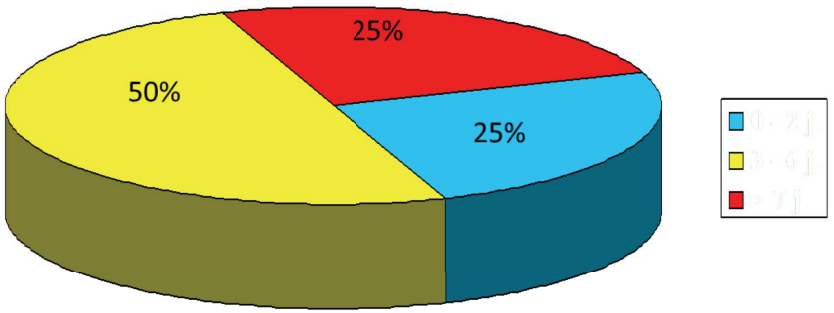


Silverman 1997, Martinez 2002

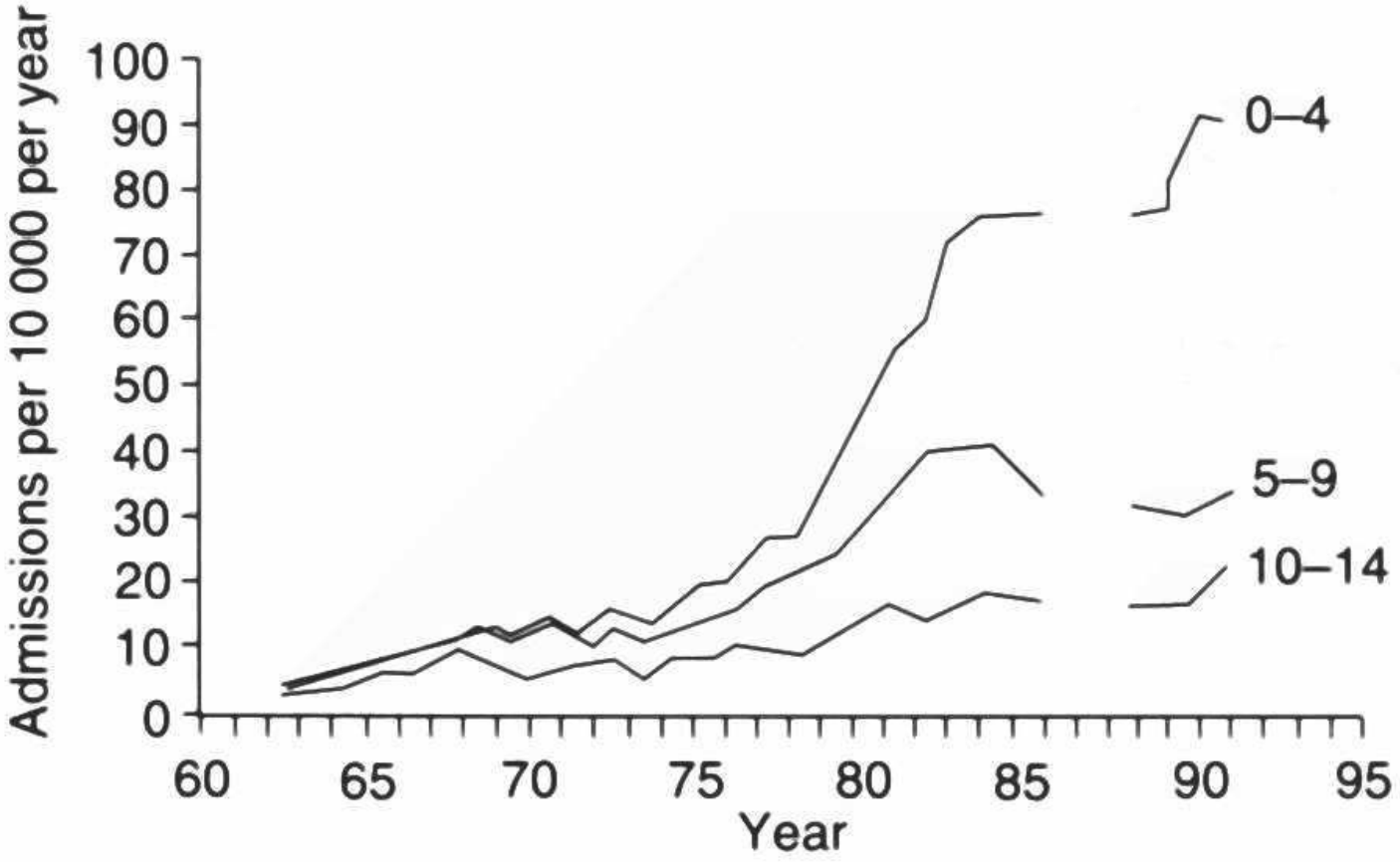
Prevalentie

- Heel frequent bij jonge kinderen
- 30% minstens 1x voor leeftijd 3 jaar

Childhood asthma: age distribution in the outpatient department



Childhood asthma
hospital admission rates



Fenotypes

Term	Definition
Temporal pattern of wheeze	
Episodic (viral) wheeze	Wheezing during discrete time periods, often in association with clinical evidence of a viral cold, with absence of wheeze between episodes
Multiple-trigger wheeze	Wheezing that shows discrete exacerbations, but also symptoms between episodes

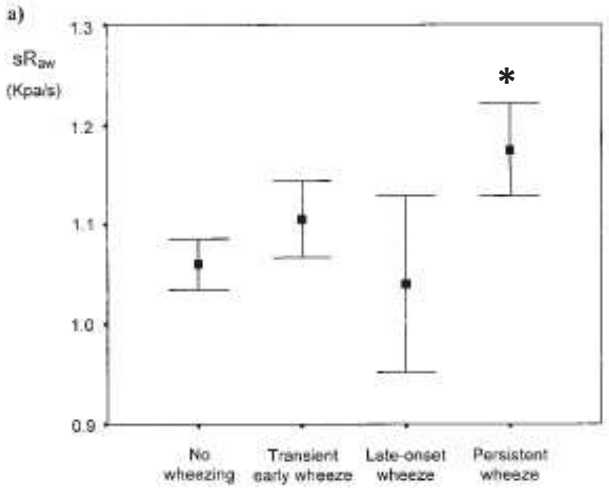
Brand, ERJ 2008

Prognose

- Prognose op jonge leeftijd moeilijk te geven:
  - zuigelingen en peuters: peuterastma: 2/3 verdwijnt tegen leeftijd 6 jaar

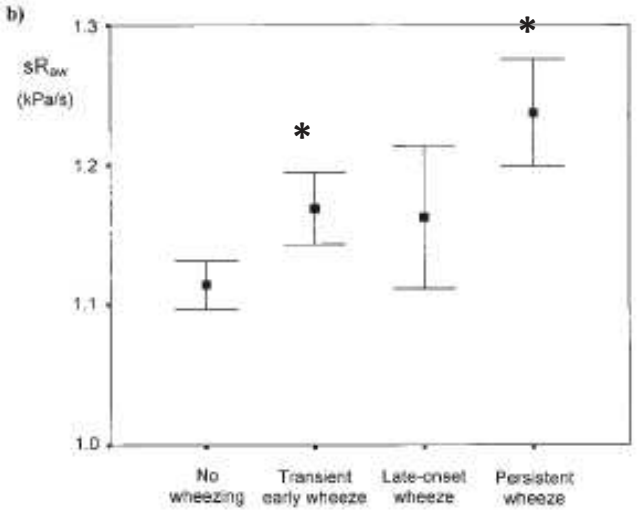
- Astma:
  - 25% klachten in eerste 6 maand
  - 75% heeft klachten voor 3 jaar

3 years



N = 463

5 years



N = 690

Lowe 2005

‘Heeft mijn kind astma?’

mAPI			
Primary	≥4 wheezing episodes in a year		
AND			
Secondary	At least 1 major:	OR	At least 2 minor:
	Parental physician-diagnosed asthma		Wheezing unrelated to colds
	Physician-diagnosed atopic dermatitis		Eosinophils ≥4% in circulation
	Allergic sensitization to at least one aeroallergen		Allergic sensitization to milk, egg, or peanuts

Modified astma predictive index

Chang, JACI 2013

Risicofactoren voor ontwikkeling van astma

- Genetische predispositie
- Atopie

Table 3. – Multivariate analysis for the persistence of early life wheezing

Risk factors	p-value	OR	95% CI
Recurrent chest infections at 2 yrs	0.034	1.99	1.05–3.77
Family history of asthma	0.010	2.31	1.22–4.37
Atopic SPT at 4 yrs	<0.001	5.73	2.95–11.12
Nasal symptoms at 1 yr	0.039	0.43	0.19–0.96

Kurukulaaratchy R.J. 2003

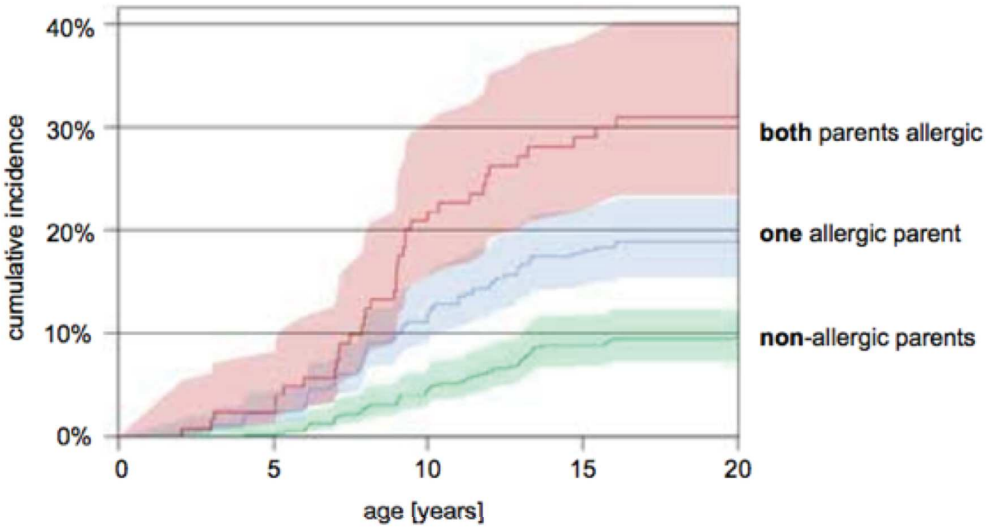


Figure 2 Family history for asthma and cumulative incidence of allergic diseases in offsprings. (*Reprinted from J Allergy Clin Immunol, 133/4, Grabenhenrich LB, Gough H, Reich A, et al. Early-life determinants of asthma from birth to age 20 years: A German birth cohort study, 979-988, Copyright 2014, with permission from Elsevier.*)

Diagnose

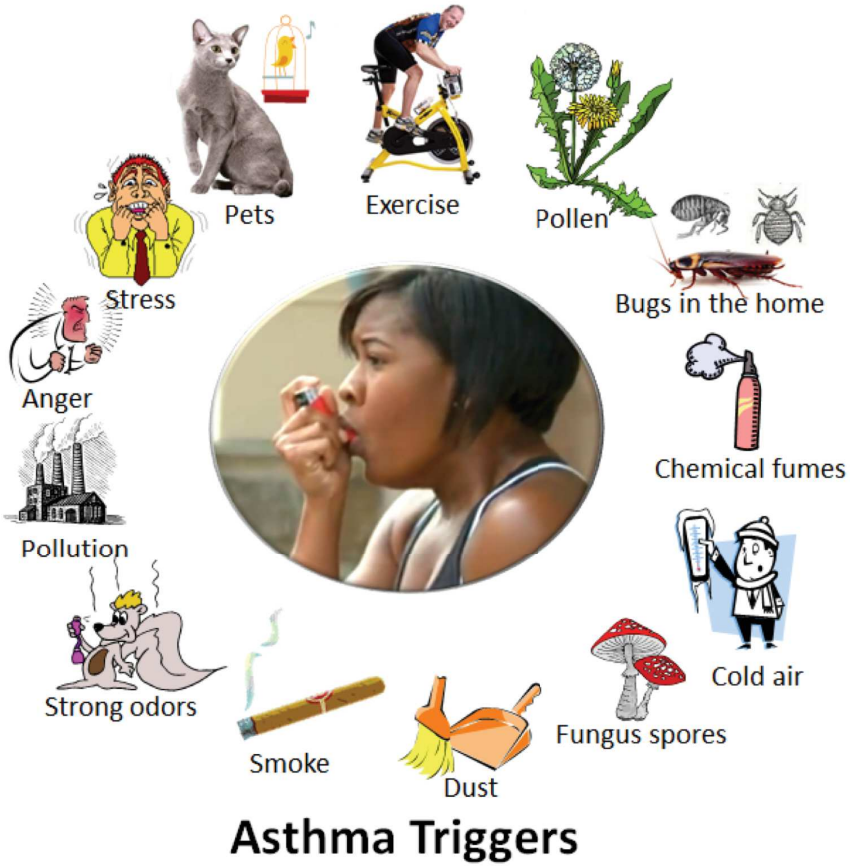
- Anamnese
- Klinisch onderzoek
- Aanvullend onderzoek
- Differentieel diagnose
- Respons op behandeling

Anamnese

- Symptomen:
  - Aard: piepen, (nachtelijk) hoesten, kortademigheid, bronchorroe
    - <2 jaar: voedingsproblemen, luide ademhaling, tirage
    - >2 jaar: vermoeidheid, schoolverzuim, inspanningsgerelateerde klachten, vermijden van activiteiten
  - Frequentie: aantal exacerbaties, recurrente/chronische klachten
  - Triggers
- Slaappatroon
- Nasale klachten
- Eczeem

Uitlokkende factoren

- Allergie
- Gastro-oesophagale reflux
- Virussen
- Inspanningen
- Niet-specifieke prikkels:
  - Koude lucht
  - Prikkelende geuren
  - Passief roken
  - Pollutie
  - Huisdieren
  - Vochtigheid/schimmels

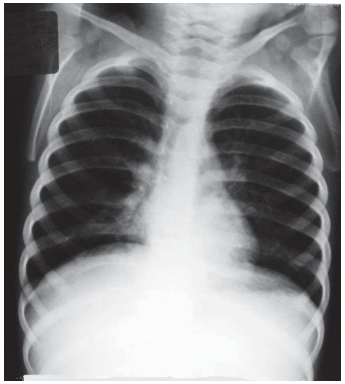


Klinisch onderzoek

- Inspectie
  - Dyspnoe, tachypnoe, ademhalingsarbeid
  - Eczema
- Auscultatie
  - Piepen, verlengd expirium, verminderd inkomend ademgeruis
- NKO-onderzoek, cervicale klieren, …

Aanvullend onderzoek

- Astma = klinische diagnose
- Uitsluiten van andere ziektes: obv. anamnese of igv. treatment failure
  - RX thorax
  - 24u-pHmetrie
  - Zweettest
  - Bronchoscopie
- Allergie
  - Bloedafname
  - Huidpriktesten
- Longfunctie: vanaf 6 jaar



Differentiaaldiagnose

- Virale infecties
- Gastro-oesophageale reflux
- Mucoviscidose / PCD
- Vreemd voorwerp aspiratie
- Congenitale afwijkingen van de luchtwegen
  - Tracheo-/bronchomalacie
  - Vasculaire compressie
- Bronchopulmonale dysplasie
- Immuundeficiëntie
- …

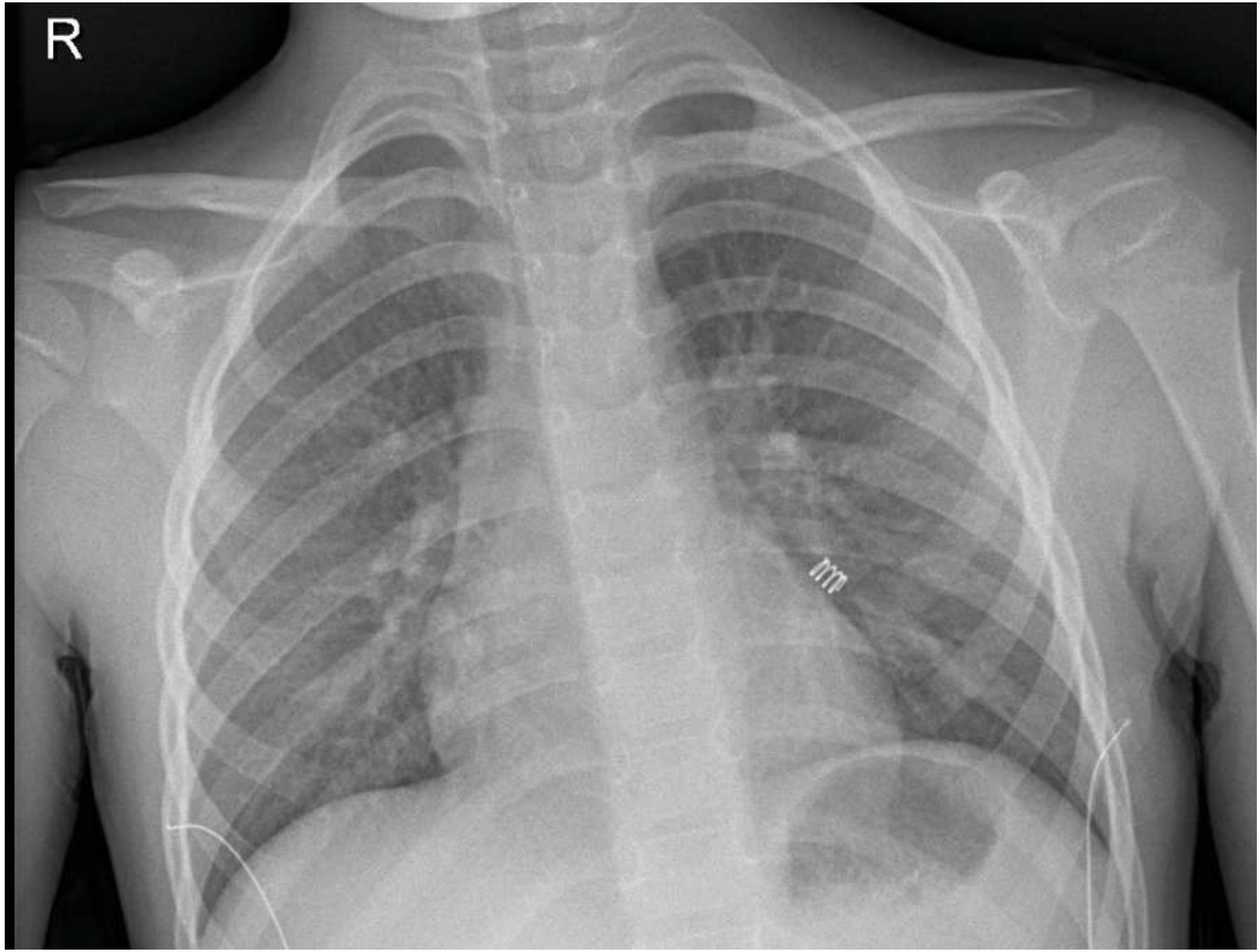
Table 1

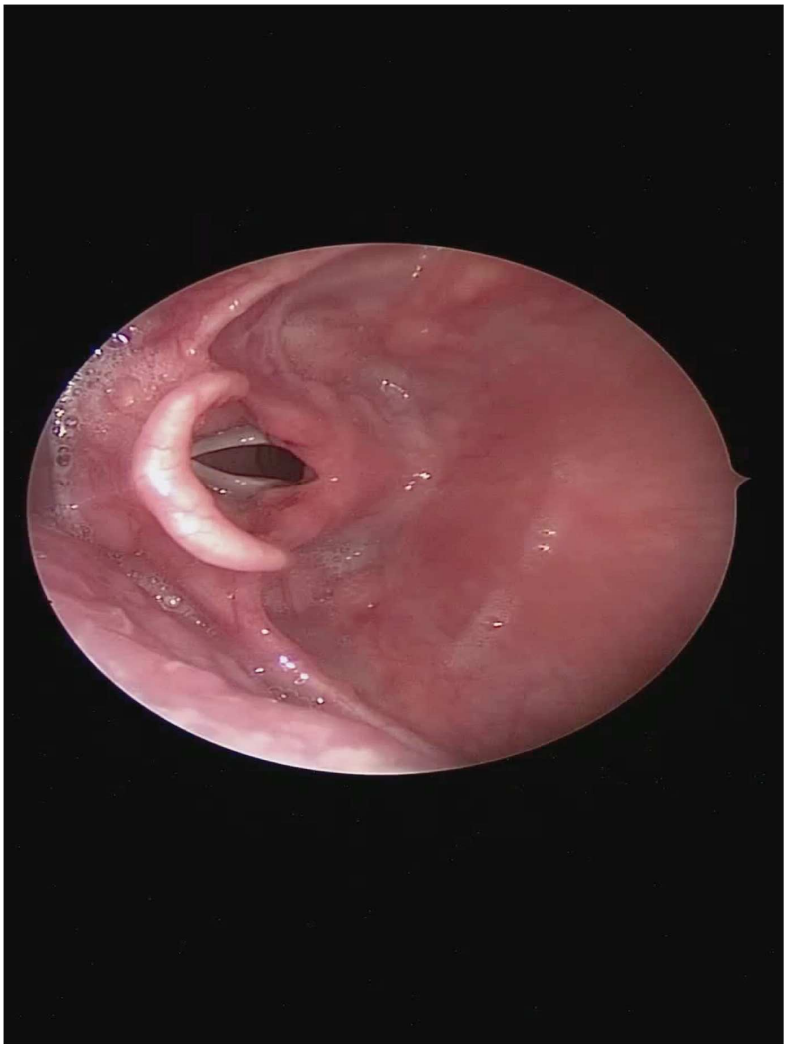
Clinical clues to alternative diagnosis in children with wheezing.

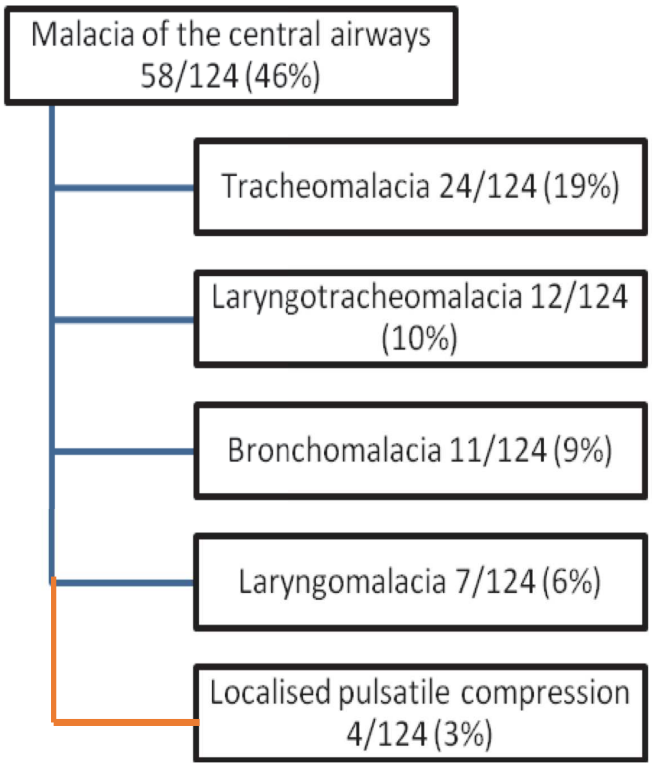
Clinical clue	Possible diagnosis
PERINATAL AND FAMILY HISTORY	
Symptoms present from birth	Chronic lung disease of prematurity, PCD, CF
Family history of unusual chest disease	CF, Neuromuscular disorders, PCD
Severe upper respiratory tract disease	PCD
SYMPTOMS AND SIGNS	
Persistent moist cough	PBB, Bronchiectasis, Recurrent aspiration, PCD, CF
Excessive vomiting	GERD (w/without aspiration)
Dysphagia	Swallowing problems (w/without aspiration)
Breathlessness with light headedness and peripheral tingling	Dysfunctional breathing, Panic attacks
Inspiratory stridor	Tracheal or laryngeal disorder
Abnormal voice or cry	Laryngeal problems
Focal signs in chest	Developmental anomaly, FB, Post-infective syndrome
Persistent wheeze	Extrinsic intra thoracic airway compression, Airway-malacia, Luminal obstruction, CF, FB
Finger clubbing	CF, Bronchiectasis
Failure to thrive	CF, GERD

CF, cystic fibrosis; FB, foreign body; GERD, gastro-esophageal reflux disease; PBB, protracted bacterial bronchitis; PCD, primary ciliary dyskinesia.

Ullman 2018


R



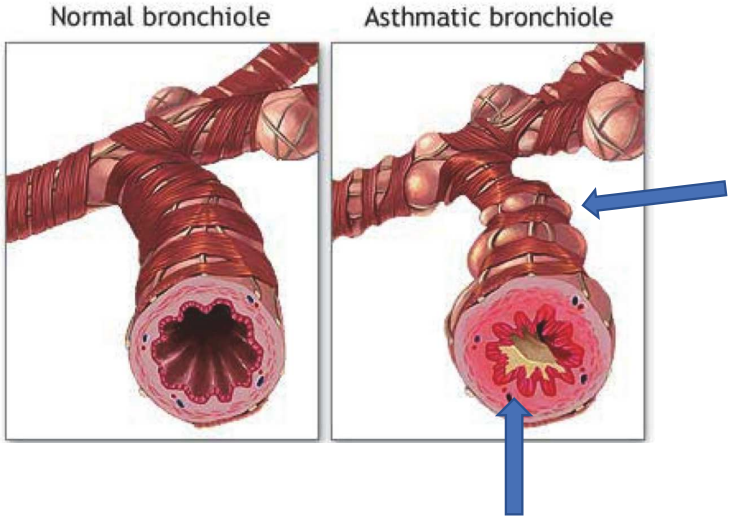


European Respiratory Journal 2011

Behandeling

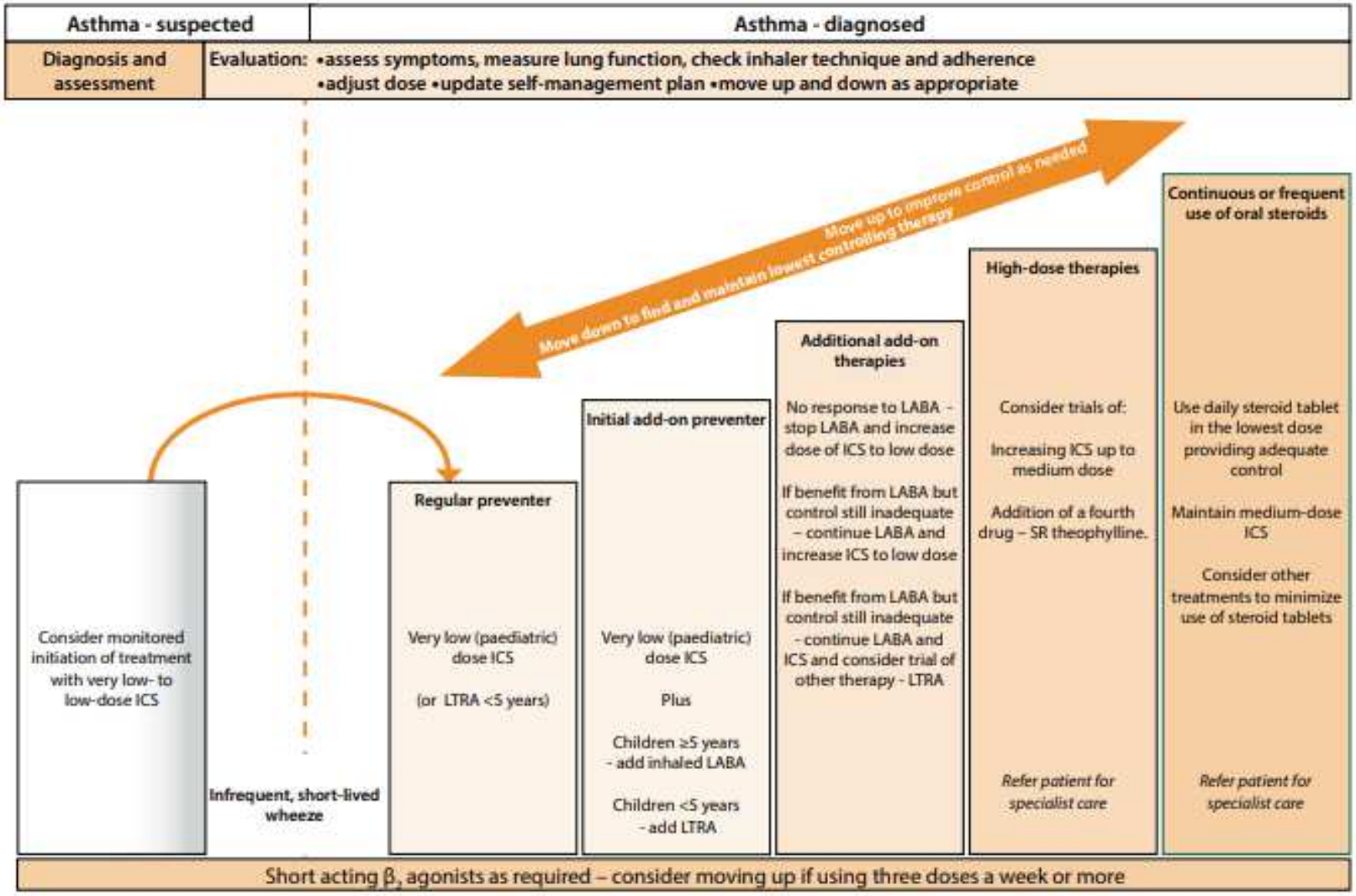
- Preventie!

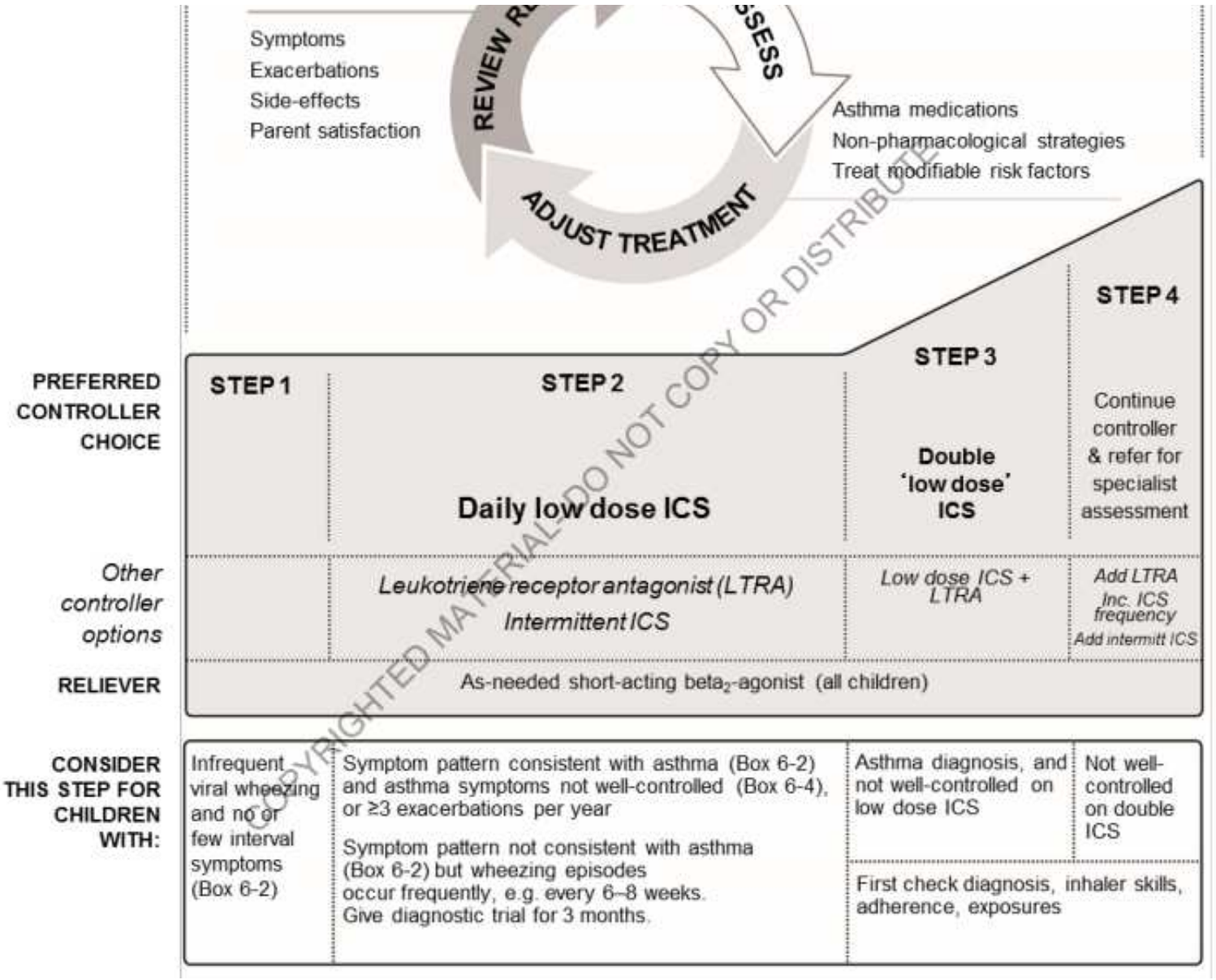
- Farmacotherapie
  - Onderhoudsbehandeling
  - Noodbehandeling



Preventie

- Mijden van triggers
  - Passief roken
  - Virale infecties
  - Allergenen
  - Gastro-oesophageale reflux behandelen


Asthma - suspected
Asthma - diagnosed
Diagnosis and assessment
Evaluation: •assess symptoms, measure lung function, check inhaler technique and adherence
•adjust dose •update self-management plan •move up and down as appropriate
Move up to improve control as needed
Move down to find and maintain lowest controlling therapy
Consider monitored initiation of treatment with very low- to low-dose ICS
Infrequent, short-lived wheeze
Regular preventer
Very low (paediatric) dose ICS
(or LTRA <5 years)
Initial add-on preventer
Very low (paediatric) dose ICS
Plus
Children ≥5 years - add inhaled LABA
Children <5 years - add LTRA
Additional add-on therapies
No response to LABA - stop LABA and increase dose of ICS to low dose
If benefit from LABA but control still inadequate – continue LABA and increase ICS to low dose
If benefit from LABA but control still inadequate - continue LABA and ICS and consider trial of other therapy - LTRA
High-dose therapies
Consider trials of:
Increasing ICS up to medium dose
Addition of a fourth drug – SR theophylline.
Refer patient for specialist care
Continuous or frequent use of oral steroids
Use daily steroid tablet in the lowest dose providing adequate control
Maintain medium-dose ICS
Consider other treatments to minimize use of steroid tablets
Refer patient for specialist care
Short acting β2 agonists as required – consider moving up if using three doses a week or more



Gina 2018

Inhalatiecorticosteroiden

- Eerste keuze behandeling

- Actieve producten:
  - Budesonide (Pulmicort®, Miflonide®)
  - Fluticason (Flixotide®)
  - Beclomethasone (Qvar®, Beclophar®)

- Bijwerkingen
  - Lokaal: spruw, heesheid
  - Systemisch: groeivertraging, hypertensie, diabetes, osteoporosis, obesitas, moonface, acne, glaucoom, …

LTRA: Montelukast

- Add-on bij ICS
- Alternatief voor mild astma (monotherapie) of bij viraal geïnduceerd wheezing
- Alternatief bij steroidfobie of contra-indicatie voor ICS

- Oraal
  - dosis afhankelijk van leeftijd
    - 4mg 2-5j
    - 5mg 5-15j
    - 10mg >15 j
  - 1x/d weg van maaltijden

- Bijwerking:
  - Hoofdpijn
  - Buikpijn
  - Nachtmerries

LABA: langwerkende β2- mimetica

- Formoterol (effect binnen de 5 minuten, duur: 12u)
  - Kan ook in acute crisis helpen
- Salmeterol (effect na 20 min, duur: 12u)
  - Neiging tot betere astmacontrole tov Formoterol

- Nooit in monotherapie!! Altijd + ICS

- Voorbehouden voor ernstig astma
- Geen gegevens < 5jaar, vnl. kinderen >12 jaar
- Weinig bijwerkingen (tremor, duizeligheid)

Wanneer behandelen?

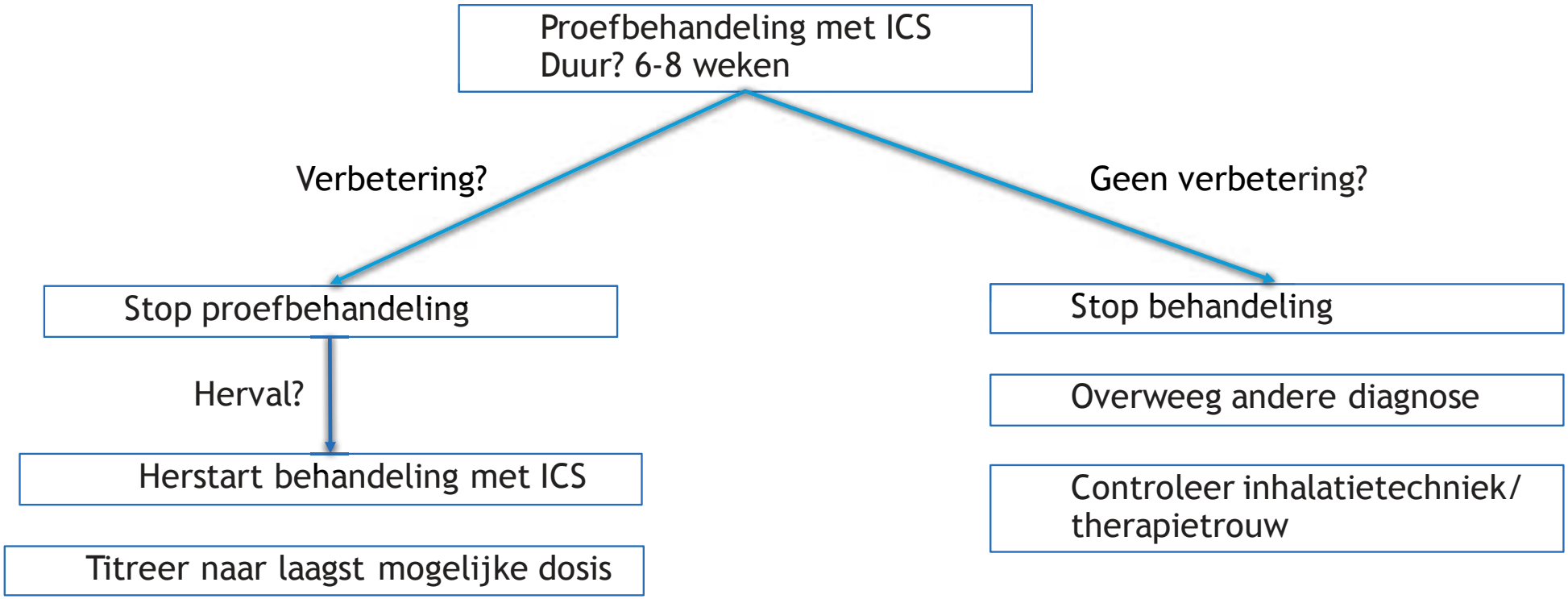
- Episodic viral wheeze
- Geen wheezing tussen verkoudheden

Intermittente behandeling met SABA
Duur? Min. 1w of 48u symptoomvrij

Wanneer behandelen?

- Multiple trigger wheeze
- Ernstige klachten van wheezing (> 1 episode/maand, >3 episoden/6 maand)
- Ziekenhuisopnames / hypoxie
- Inspanningsgebonden klachten / nachtelijk hoesten / familiale atopie

Proefbehandeling met ICS
Duur? 6-8 weken


Proefbehandeling met ICS
Duur? 6-8 weken
Verbetering?
Geen verbetering?
Stop proefbehandeling
Herval?
Herstart behandeling met ICS
Titreer naar laagst mogelijke dosis
Stop behandeling
Overweeg andere diagnose
Controleer inhalatietechniek/ therapietrouw

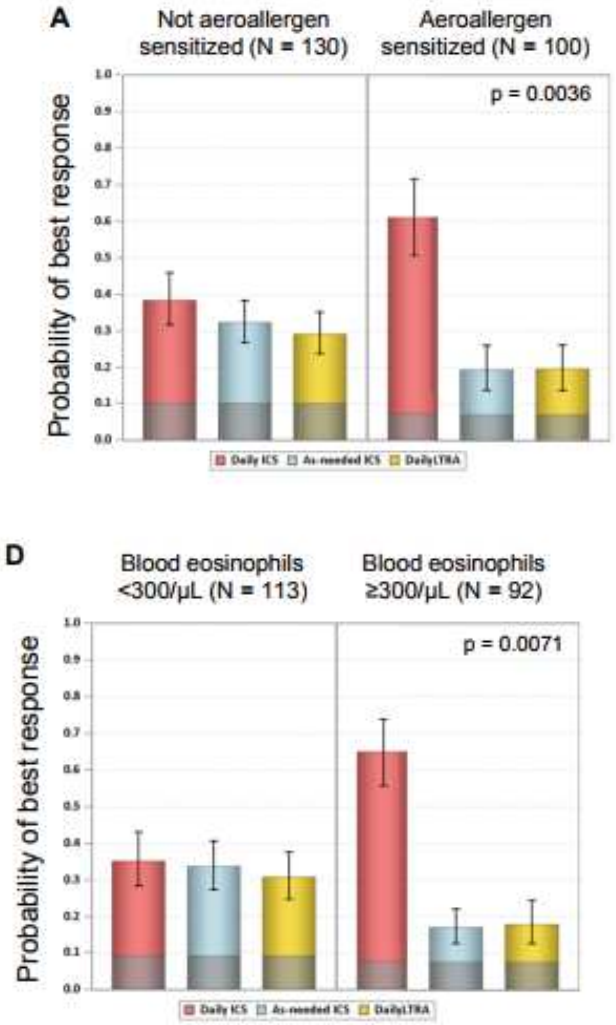
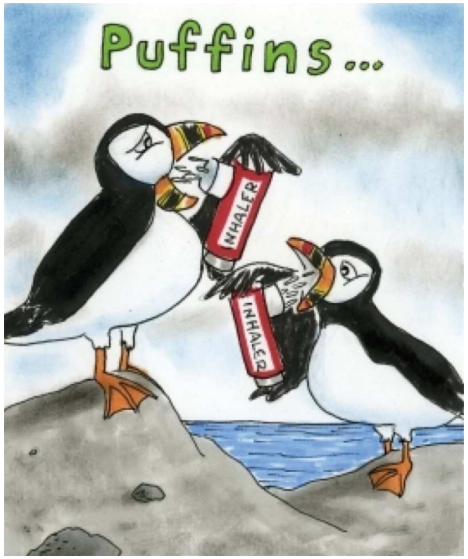


FIG 4. Probability of best response based on aeroallergen sensitization **(A)**, previous exacerbation **(B)**, sex **(C)**, eosinophil count of 300/μL or greater **(D)**, and combination of sensitization and eosinophil counts **(E)**. *P* values correspond to the test of interaction between the predictor and treatment and indicate whether the pattern of treatment response differs according to subgroup. Sample sizes correspond to participants with evaluable data (n = 230).

Fitzpatrick 2016

Inhalatietherapie

- Correcte techniek heel belangrijk
- Afhankelijk van
  - Leeftijd
  - Inspiratoire flow
  - Frequentie dosissen
  - Activiteiten, school



Inhalatiemethoden

- Aerosol
- Doseeraerosol + voorzetkamer (met masker of mondstuk)
- Autohaler
- Droogpoederinhalator

Written and practical tests on inhaler techniques

Table 3. Mean ± SD Scores by Profession

	RTs ($n = 20$)	Pharmacists ($n = 8$)	RNs ($n = 21$)	Physicians ($n = 14$)
Written				
Before	70.0 ± 11.4*	78.3 ± 18.9	60.5 ± 14.0	54.2 ± 11.1
After	71.9 ± 7.9	81.7 ± 20.2	63.5 ± 12.7	55.8 ± 12.4
Practical				
Before	77.3 ± 12.2*	77.2 ± 8.0	67.4 ± 15.8	56.1 ± 8.6
After	83.6 ± 10.6†	82.5 ± 1.5	71.6 ± 12.2	64.0 ± 16.3

$N = 63$.

* Significant difference from registered nurses and physicians.

† Significant difference between before and after.

RTs = respiratory therapists

RNs = registered nurses

Alismail 2016

Table 1 Considerations required for inhaler techniques for a variety of ages

Device	0–3 years	4–6 years	>7 years
pMDI	Unable to co-ordinate breathing	Vast majority of children and adults struggle to co-ordinate breathing with device actuation. Technique should be assessed and reviewed regularly	
pMDI with spacer	Use a small spacer with a mask. Tidal breathing required as young children are unable to take deep breaths during an attack and unlikely to be able to hold breath	Small spacer with a mouth piece. Most children achieve adequate lung deposition with two deep breaths and 5–7 s of breath holding. Needs review and if unable to perform should use the technique of 0–3 years as tidal breathing is as effective as deep breaths	Any spacer with a mouth piece. Ensure ability to take one deep breath and hold breath for 7 s. Needs review and if unable to perform should use the technique of 0–3 years as tidal breathing is as effective as deep breaths
DPI (eg, Turbohaler, Accuhaler and Easyhaler)	Insufficient inspiratory flow to activate the device. Unable to teach breath holding	When well children may have sufficient inspiratory flow to activate the device but likely to be insufficient when unwell. Unlikely to be able to teach breath holding	Avoids need for device-breath co-ordination. Ensure ability to take a quick forceful deep breath. Needs review to ensure ability to hold breath for 5–7 s post dose
Breath actuated inhaler (eg, Easi-Breathe inhalers and Autohalers	Unlikely to achieve lung deposition due to short and limited inspiratory flow. Unlikely to be able to teach breath holding		Requires normal deep inhalation. Needs review to ensure ability to hold breath for 5–7 s post dose

Adapted from van Aalderen *et al*.[13]
DPI, dry powered inhalers; pMDI, pressurised metered-dose inhaler.

Inhalatietechnieken

- <2j: aërosol/ doseeraërosol via voorzetkamer met masker
- 2-4j: aërosol in acute fase / doseeraërosol via voorzetkamer met masker in onderhoud
- 4-6j: doseeraërosol via voorzetkamer met mondstuk/ Autohaler / Droogpoederinhalator
- >6j: Droogpoederinhalator

Aërosol

- Op elke leeftijd
- Wanneer spacer onmogelijk is (CP-patiënt, angst)
- Acute situatie (tachypnoe)
- Gelijktijdige toediening O2 mogelijk

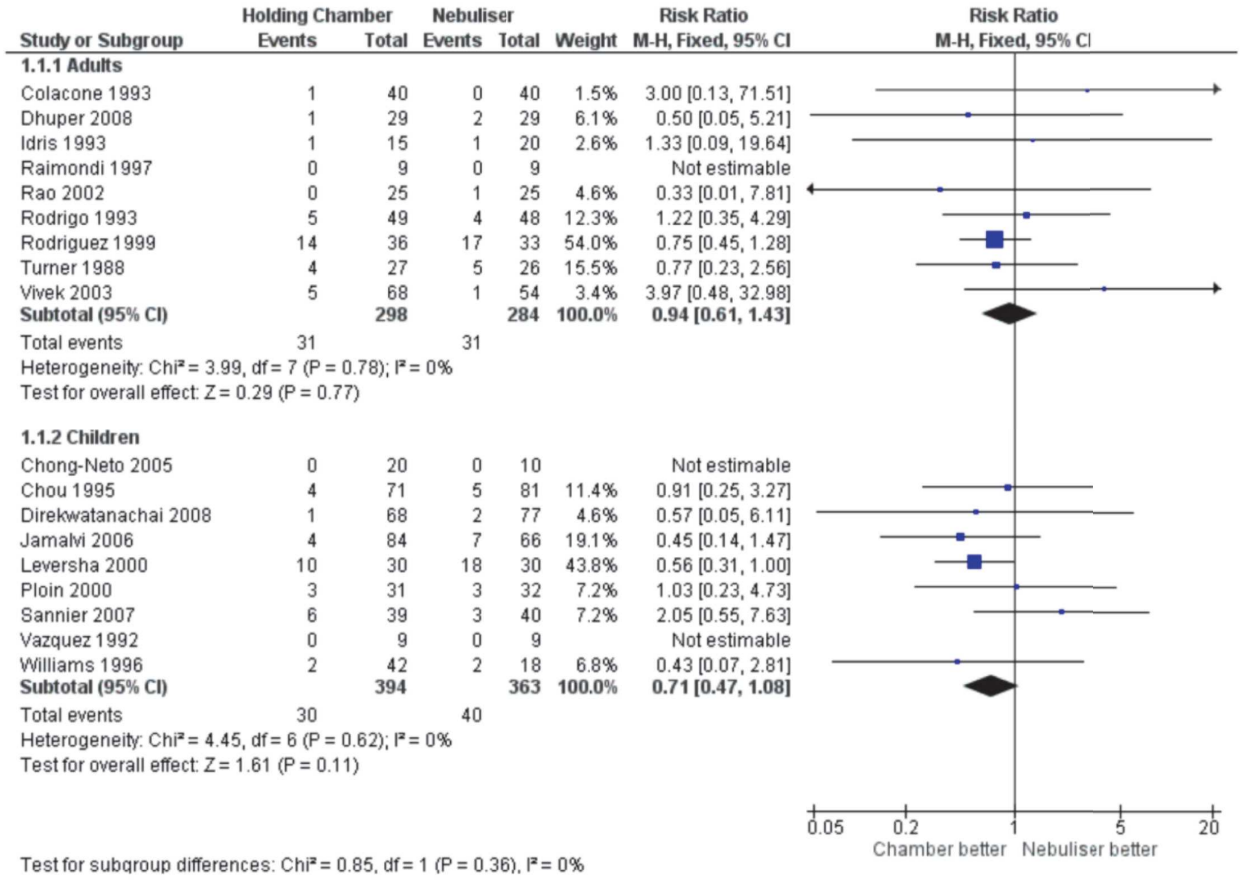
- Werkelijke dosis toegediend = ?
- Natte aerosol → infectierisico
- Tijdrovend
- Onhandig

Doseeraërosol

- Gestandardiseerde dosis
- Voor alle leeftijden
- Minder medicatieverlies
- Minder orofaryngeale depositie
- Betere therapietrouw

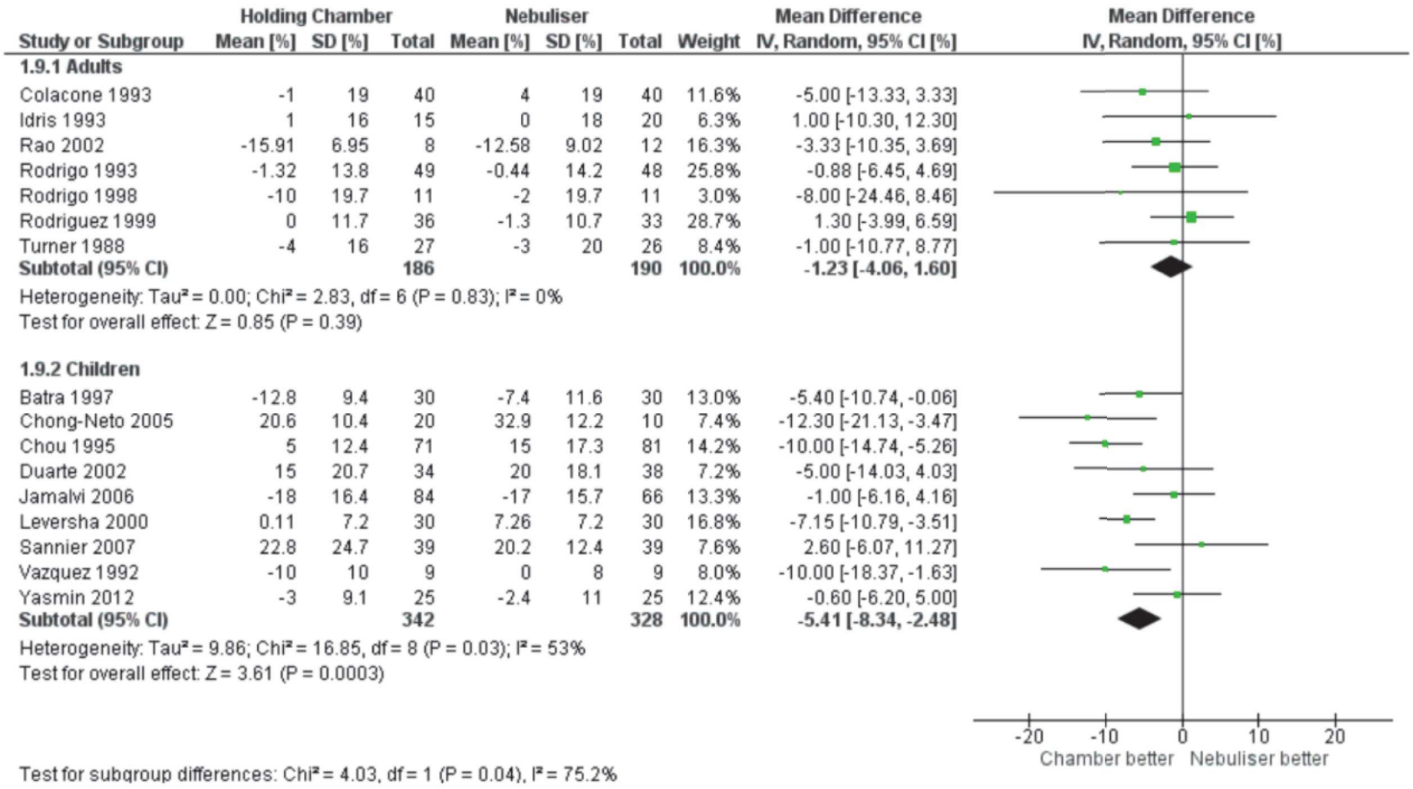
- Techniek belangrijk
- Geen uniformiteit spacers
- Minder goed verdragen bij dyspnoe

Figure 4. Forest plot of comparison: 1 Spacer (chamber) versus Nebuliser (Multiple treatment studies), outcome: 1.1 Hospital admission.



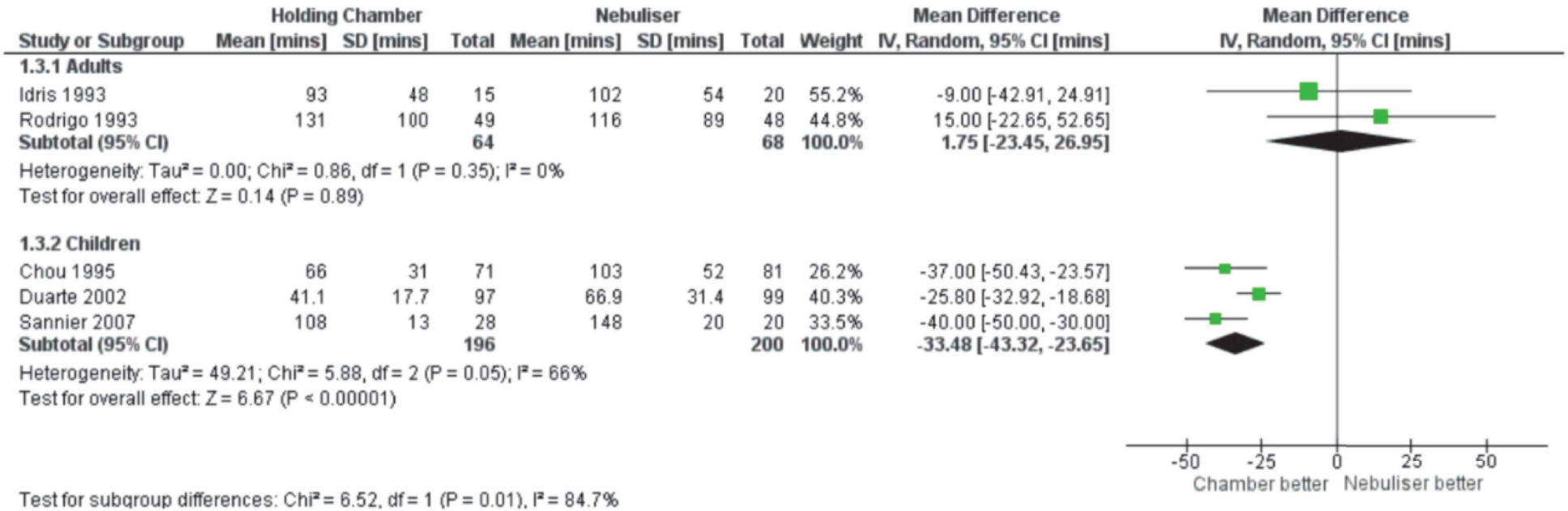
Cates 2013 Cochrane review

Figure 6. Forest plot of comparison: 1 Spacer (chamber) versus Nebuliser (Multiple treatment studies), outcome: 1.9 Rise in pulse rate (% baseline) [%].



Cates 2013 Cochrane review

Figure 5. Forest plot of comparison: 1 Spacer (chamber) versus Nebuliser (Multiple treatment studies), outcome: 1.3 Duration in emergency department (minutes). [mins].



Cates 2013 Cochrane review

Autohaler

- Geen spacer nodig
- Gebruiksvriendelijk
- Diepere longdepositie door kleinere deeltjesgrootte

- Vanaf +/- 6 jaar
- Niet voor alle astma-medicatie
- Orale depositie

Droogpoederinhalator

- Geen spacer
- Geen gas
- Gebruiksvriendelijk en discreet

- Hoge inspiratoire kracht nodig
- Orale depositie
- Opgelet bij lactose-intolerantie
- Moeilijk bij acute aanval

Types droogpoederinhalatoren

- Aerolizer
  - Foradil®, Miflonide®, Beclophar®
- Discus
  - Flixotide ®, Serevent®, Seretide®
- Novolizer
  - Novolizer Budesonide®, Novolizer Salbutamol®, Novolizer Formoterol ®
- Turbohaler
  - Bricanyl®, Pulmicort®, Oxis®, Symbicort®

Take home message

- Wheezing is not always asthma
- Astma-behandeling kan soms aangewezen zijn
- Bij onbevredigende respons op ICS: denk aan alternatieve oorzaken
- Correcte inhalatietechniek en educatie van patiënt zeer belangrijk