The Impact of Asthma and Wheeze in Children

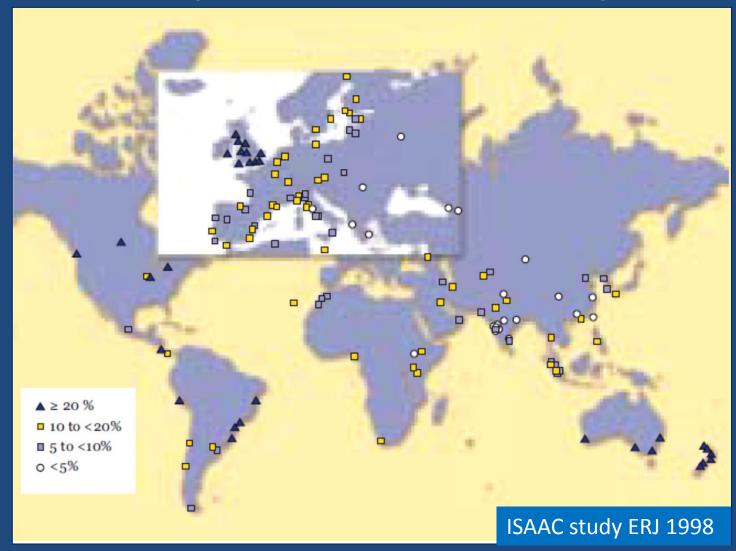
Asthma and Wheeze in Children Pharmac Workshop 2015



Asthma and Wheeze are Common

- Incidence of "current wheeze" 20 28% NZ children
- Nearly half a million NZers on asthma medication
- Cost of hospitalisations \$800 million per year
- 65-70 deaths per year

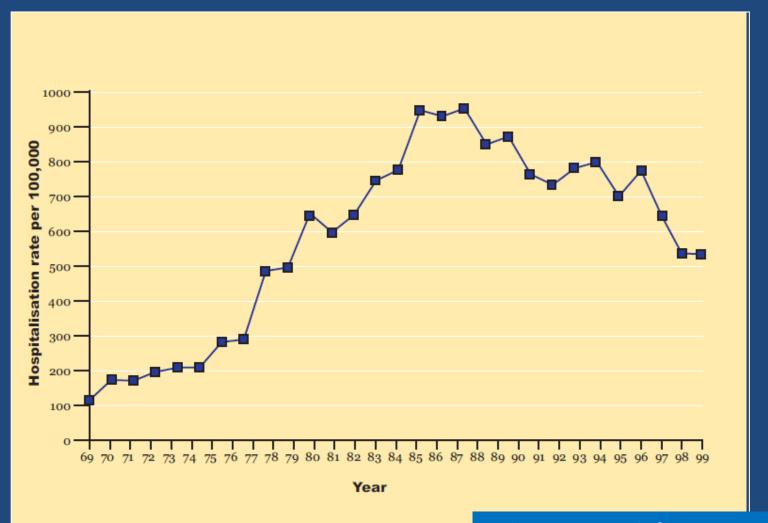
Prevalence of current wheeze related to ethnicity and social development





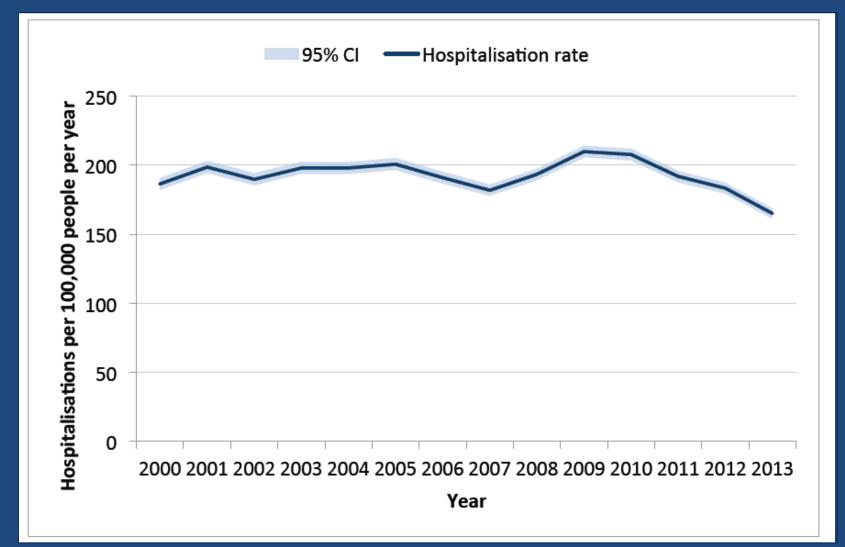
The Lancet 1998; 351: 1228

Past concerns increasing hospitalisations and mortality



Holt, P3 research for ARFNZ, 2001

More stable in recent years



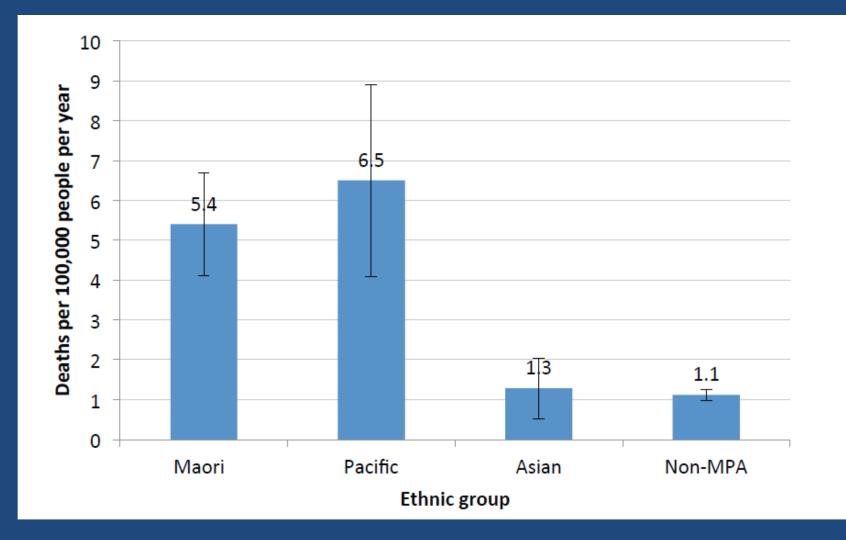
Impact of Respiratory Disease In NZ: 2014 Update, Asthma Foundation

Impact of Asthma not evenly spread

- Maori & Pacific 3x as likely to be hospitalised
- Most deprived areas 3.2x more likely to be hospitalised than least deprived

 Continues to increase in third world countires as they become modernised

Asthma mortality



Despite this there are also treatment disparities

- Maori and Pacific children more likely to receive oral steroids and nebulisers
- But less likely to receive ICS
- Less likely to receive asthma education
- Less likely to be given an action plan

Crengle, Thesis 2008 Gillies, Prim Care Resp J 2013

Summary

- Asthma and wheeze are common
- Ethnic disparities in incidence, severity and treatment



What is asthma?

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Current definition

- A chronic (lifelong) disorder
- Inflammatory disorder
- Characterised by respiratory symptoms

 Wheeze, cough, shortness of breath
- Plus variable airflow obstruction

What is wheeze?

- A high-pitched, musical, adventitious lung sound produced by airflow through narrowed airways.
- Indicates abnormal airflow through a narrowed airway
 - Acute/chronic
 - Monophonic/polyphonic

What do parents mean when they use the word wheeze?

- Parents may use "wheeze" for a variety of infant noisy breathing
- Only 59% can correctly identify wheeze
- Agreement between doctors and parents < 70%

 Other noises may imply upper airway or tracheal pathology

> Elphick, Arch Dis Child 2001 Cane, Arch Dis Child 2001

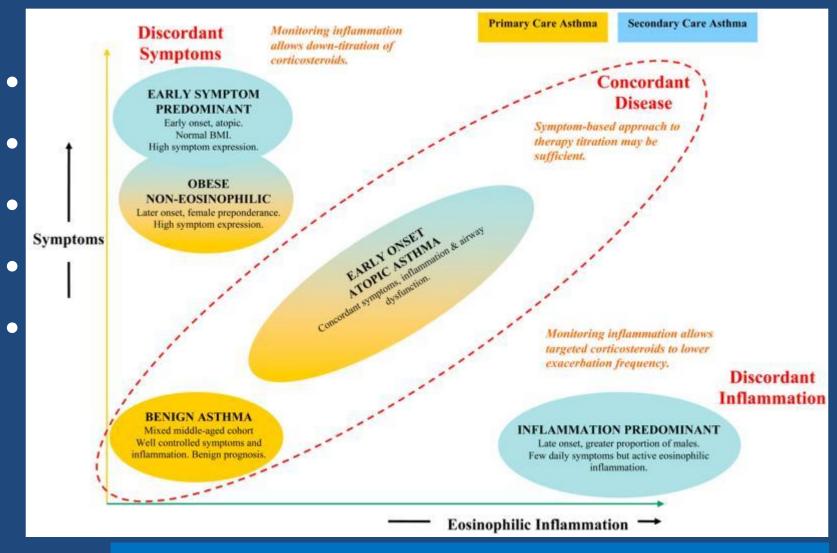
Pathophysiologic features of asthma

- Bronchoconstriction
- Inflammatory infiltrate
- Airway remodelling
- Airway oedema
- Mucus hypersecretion

Why do we need phenotypes of asthma?

- Treatment
- Prognosis
- Children may be different

Multiple phenotypes of adult asthma:



Halder et al, Am J Respir Crit Care Med. Aug 1, 2008; 178(3): 218–224

Why separate children into phenotypes?

- Currently separate children into
 - School age asthma
 - Pre-school Wheeze
- 50% of preschoolers will have wheeze before age 5 years
- Only 1/3 of these will have current wheeze at school age
- Different response to therapy
- Which pre-schoolers will go on to have asthma?

Diagnosis of asthma in children

- Clinical diagnosis
 - Symptoms
 - Likelihood
 - Supportive testing
 - Response to therapy
- With careful consideration of alternative diagnoses

Helpful Features For Asthma Diagnosis

- Specificity of symptoms
- Hayfever or eczema
- Family history of atopy
- Blood eosinophilia

Red Flags

- Daily or constant symptoms
 - -Wheeze or stridor every day
 - Daily wet or moist cough
- Failure to thrive
- Chest wall deformity
- Digital clubbing
- Skin or other infections



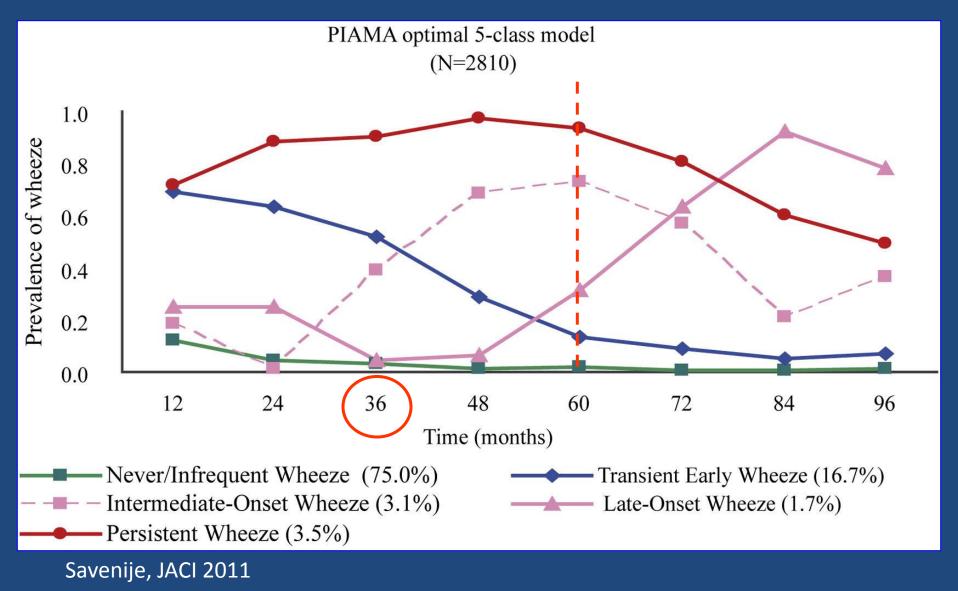
Diagnostic tests are not necessarily helpful

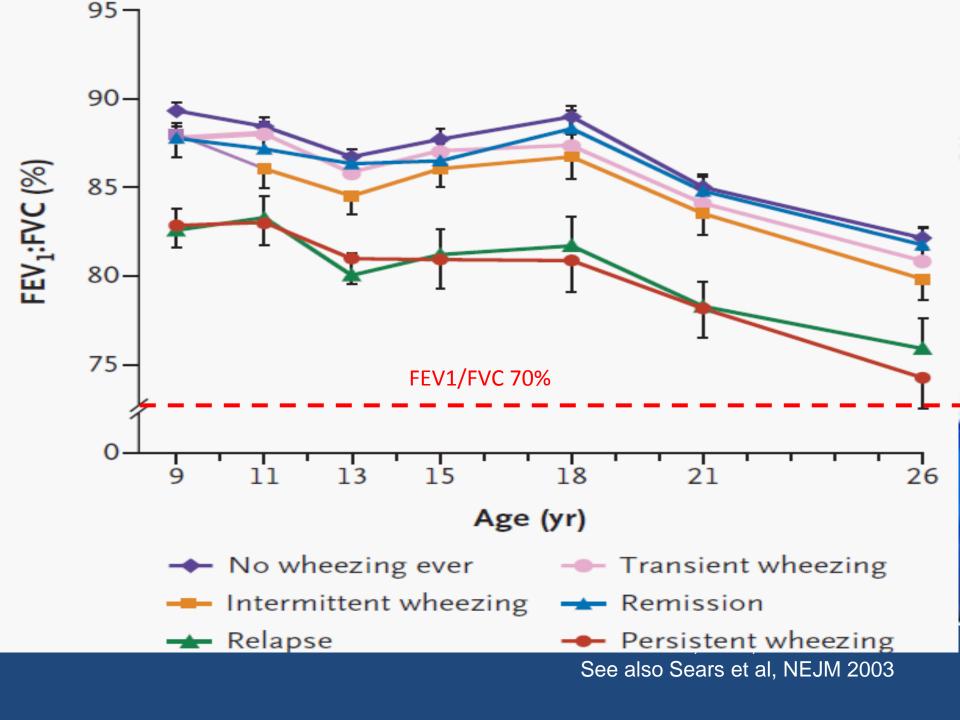
- Spirometry
- Bronchodilator response
- Exercise challenge
- Inhalational challenge
 - Methacholine, hypertonic saline, Mannitol

What is preschool wheeze?

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Patterns of preschool and childhood wheeze

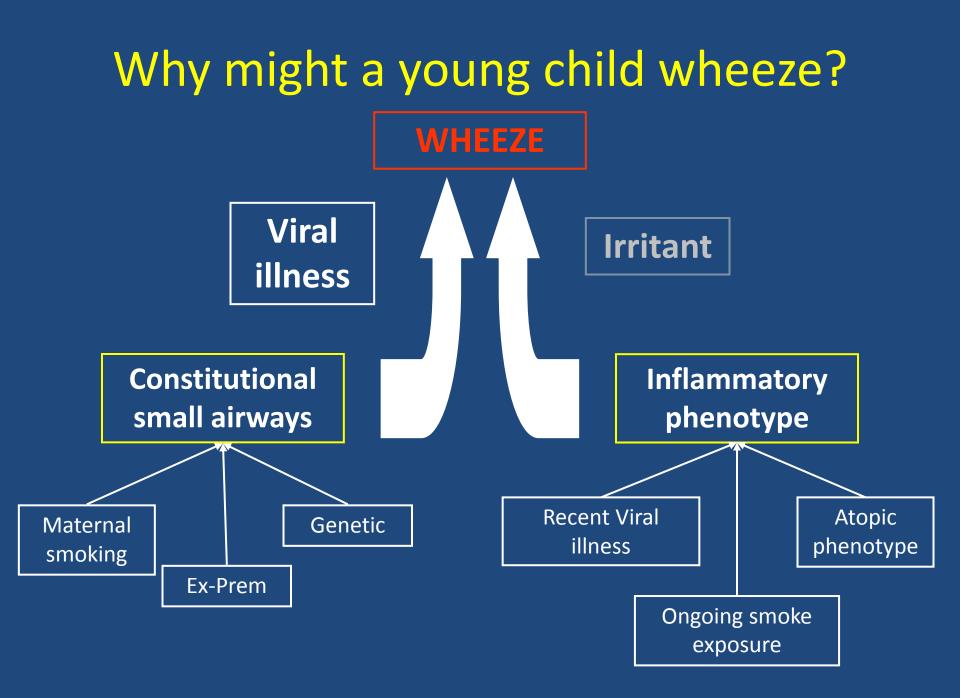




Pre-School Wheeze

- Different from adult asthma
- Different inflammatory profile in infants
 Even in those with subsequent asthma
- Different management

 Not all pre-schoolers with wheeze go on to have asthma



Two Main Groups

- Those who only wheeze with viral exacerbations
 - No persisting inflammation
- Those who have symptoms between exacerbations
 - Persisting inflammation
 - "multi-trigger wheeze"
- May switch between groups
 - ?post viral inflammation/responsiveness
 - Treatment trials for 3 months only
 - Schultz Acta Paediatrica 2009

Helpful Key Features

- Interval symptoms
 - -GINA questions
 - -Asthma control questionnaires
- Response to therapy

- Eczema or hayfever
- Family history of atopy

Red Flags

- Daily or constant symptoms
 - Infant with wheeze every day since birth
 Daily wet or moist cough

- Failure to thrive
- Digital clubbing
- Chest wall deformity



Control questions

- In a usual week, how many days per week:
 - Wheeze?
 - Use blue inhaler?
 - Wake at night with wheeze or cough?
- Exercise capacity
- Emergency GP, ED or hospital visits in last 12 months

Why are the phenotypes important?

• ICS cause decrease in growth

- ICS control interval symptoms
- But ICS do not control exacerbations in preschoolers
 - →Only multi-trigger wheeze will respond

Preventative management of preschool wheeze

• Episodic wheeze only

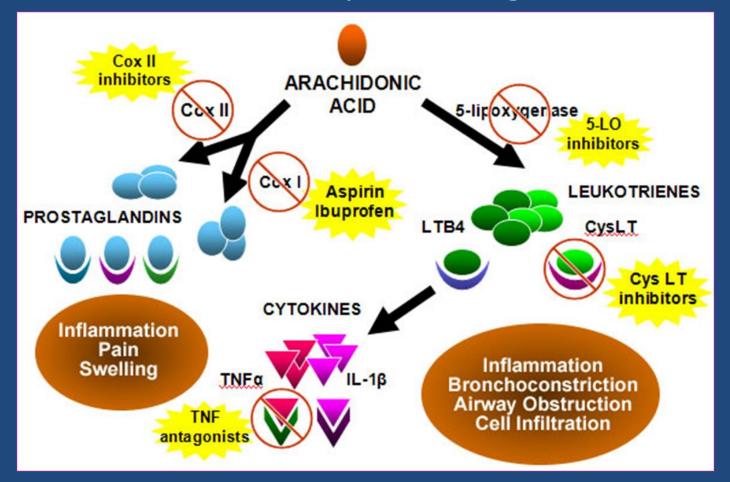
Add montelukast

- Multi-trigger wheeze

 Treat for 3 months with ICS
 Trial without ICS each 3 months
 Add montelukast if ongoing exacerbations
- Review every 3 months as may switch

What is Montelukast?

• Anti-leukotriene receptor antagonist



Advantages of Montelukast

- Cheap
- Small chewable tasty tablet
- Treats rhinosinusitis as well
- Effective in young children
 - ICS are often not
- Compliance
 - Oral medications 60-75% vs Inhaled medications 25-30%
- Minimal adverse effects
 - Same rate as placebo
 - Behavioual change/poor sleep

Disadvantages of Montelukast

- On average not quite as good as an ICS or nasal steroid
- Possible risk of Churg-Strauss

Montelukast Daily use (all studies mild to moderate)

- Improved symptoms and control
 - Knorr et al Pediatrics 2001
- Similar effectiveness to fluticasone or cromolyns
 - Davies Clin Ther 2004
- Improved peripheral eosinophils
 - Knorr 2001, Kooi Ped Pharm Ther 2008
- Improved airway hyper-responsiveness
 - Moeller, Ped Pulm 2008, Hakim Chest 2007
- Reduced exacerbations
 - Bisgaard AJRCCM 2005

Montelukast Intermittent Use

- Potentially of benefit first sign of an URTI
- Reduced symptoms and days off childcare
 - Robertson et al AJRCCM 2007
- Conflicting data that it may be effective in bronchiolitis and post-bronchiolitis wheeze
 - Definition bronchiolitis age < 2-3 yr
 - Kim et al J Peds 2010
 - Bisgaard AJRCCM 2003

• OVERALL: more evidence for continuous use

Who is Montelukast good for?

- Effectiveness vs funding
- Prevention of exercise induced wheeze
- Treatment of pre-school wheeze
 Regular or episodic treatment
- First-line preventer instead of ICS
- Good if hayfever + asthma
- Add-on to ICS (as an alternative to LABA)
- ?Add-on to ICS/LABA combination

How is Montelukast funded?

- Special authority criteria
- Pre-school
- School age and adult
- Aspirin desensitisation

Pre-school wheeze criteria

- Intermittent severe wheeze
- AND has had at least 3 exacerbations in the past 12 months severe enough to seek medical attention

School age/adult

Funded for exercised induced bronchoconstriction (EIB)

- Patient has been trialled on max ICS/LABA
- AND remains on ICS
- AND Continues to experience frequent EIB

Acute management of pre-school wheeze

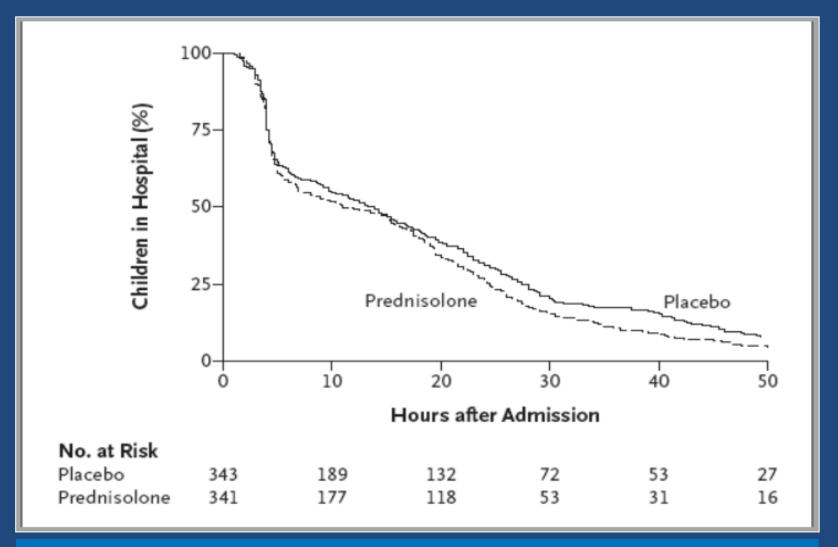
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Acute management bronchioliotis

- Children < 1 year
- The pathophysiology is not primarily bronchospasm
- Current management supportive

Acute management of pre-school wheeze

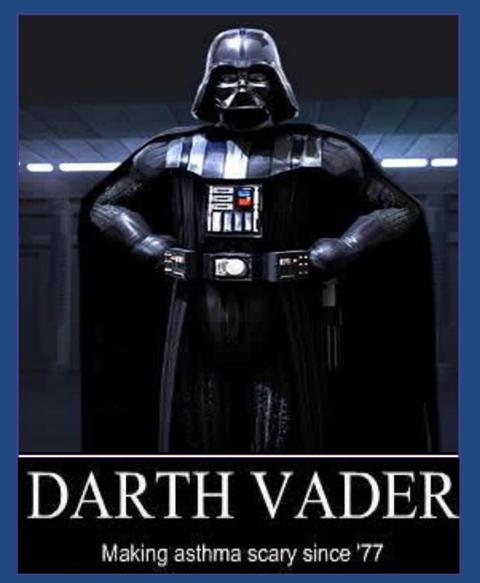
- Children 1 4 years
- Most kids will respond to salbutamol
- Oral steroids
 - At this stage there is no evidence for the effectiveness of oral steroids in children < 5 years.
 - Plus evidence of harm
 - Appropriate to use for children admitted to hospital AND on oxygen



RCT of 700 children age 10 – 60 months. No difference in 7-day symptom scores, albuterol use, or readmission.

Panickar J, Lakhanpaul M, Lambert PC, et al. Oral prednisolone for preschool children with acute virus-induced wheezing. *N Engl J Med*. 2009;360(4):329–338

Questions?



Cases: Pre-school wheeze

Case 1

- 10 month old phone consult
- Wheeze since 3 4 months of age
- Worse when feeding or playing
- Not responsive to salbutamol or atrovent
- Growing well

• What is the next question?

Case 1(2)

• Tachypnoea with wheeze all the time

- Recommended bronchoscopy
 →Airway narrowing in lower trachea
 (tracheomalacia)
- Lessons from Case 1

 Beware daily wheeze

Case 2

- Four year old girl
- 2 x previous admit with wheeze requiring IV treatment (parainfluenza 3)
- Presented acutely with wheeze, requiring ICU admit and IV treatment (rhinovirus)
- On flixotide
 - No interval symptoms except salbutamol with exercise
 - No eczema or hayfever
 - Sister with asthma
- What preventive treatment next?

Case 2 (2/2)

- Added montelukast to be given at first sign of a cold (historic prior to funding)
- Discharged from clinic but readmitted the next day
- Now on regular flixotide and regular montelukast (adult dose)
 - No interval symptoms or regular salbutamol
 - Fingers crossed

Lessons from Case 2

- Regular montelukast better than PRN
- Often cannot prevent exacerbations in this age group
- Can reduce interval symptoms/improve QOL



- 14 month old presented to PICU with severe wheeze and coryza
- Ex 34/40 infant

What question next?

Case 3 (2/2)

- Salbutamol about 2 x per week for wheeze
- Commenced on flixotide
- → resolution of interval symptoms but exacerbations continue
- For montelukast if another severe episode
- Lesson from Case 3
- Pre-schoolers with multi-trigger wheeze will benefit from flixotide



- 15 month old
- 2 presentations to ICU with coryza and wheeze past 2 months (+1 previous admit)

• What question?

Case 4

- No regular symptoms of wheeze or exercise limitation
- Commenced on montelukast (and flixotide)
- No further problems

- Lesson from Case 4
- Montelukast is effective for episodic wheeze with no interval symptoms

Discussion/Questions

