

Let's Take a Breath and Look at the Evidence: An Update on Common Pediatric Respiratory Conundrums

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Financial Disclosures

- I have no financial disclosures
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Objectives

- To discuss Albuterol dosing when managing asthma
- To evaluate steroid choice when managing asthma and croup
- To evaluate short course antibiotic therapy in children with community-acquired pneumonia (CAP)

Asthma

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Audience Question: 9-year-old 35 kg boy presents w severe asthma exacerbation. He has a hx of asthma and is on Flovent. Has had 2 puffs Alb MDI with spacer in the car on the way to your UC.

What is the maximum Albuterol you would use in this case:

- A. 5mg
- B. 10mg
- C. 15mg
- D. 20mg

Albuterol: How Much?

Asthma, *Peds in Review* -2019

	Nebulizer	MDI with spacer
Green		2 puffs pre-exercise

- 1 single Albuterol 2.5 mg/3ml vial = 4-6 puffs Albuterol MDI

Patel et al. Peds in Rev. 2019



Albuterol: How much?

Asthma, *Peds in Review* -2019

	Nebulizer	MDI with spacer
Green		2 puffs pre-exercise
Yellow	2.5 mg q4h	2-4puffs Q4h

Albuterol: How much?

Asthma, *Peds in Review* -2019

	Nebulizer	MDI with spacer
Green		2 puffs pre-exercise
Yellow	2.5 mg q4h	2-4puffs Q4h
RED		
< 10 kg	5 mg/h	
10-20kg	10 mg/h	
20-30kg	15mg/h	
>30 kg	20 mg/h	

Albuterol: How much?

Asthma, *Peds in Review* -2019

	Nebulizer	MDI with spacer
Green		2 puffs pre-exercise
Yellow	2.5 mg q4h	2-4puffs Q4h
RED		
< 10 kg	5 mg/h	4 puffs Q 20m X 3
10-20kg	10 mg/h	6 puffs Q 20m X 3
20-30kg	15mg/h	6 puffs Q 20m X 3
>30 kg	20 mg/h	8 puffs Q 20m X 3

Albuterol: How much?

Asthma, *Peds in Review* -2019

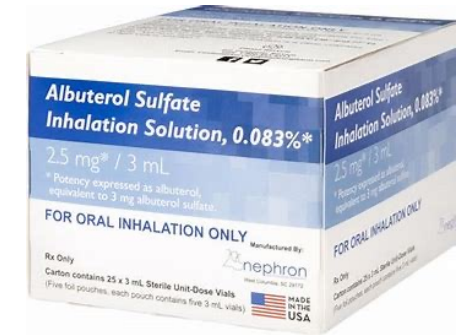
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1 single Albuterol 2.5 mg/3ml vial = 4-6 puffs Albuterol MDI

Patel et al. *Peds in Rev.* 2019

Albuterol: The Evidence

- Internet based survey of 43 children's hospitals around the country to establish what providers are actually doing: up to 25mg/hr
- National Asthma Education and Prevention Program (NAEPP) Expert Panel 2:
 - 0.15 mg/kg Alb X 3 [min 2.5mg]
 - Then 0.15-0.3 mg/kg Alb q1 [max 10 mg]
 - 0.5 mg/kg Alb continuous
- Patel SJ, Teach SJ. Asthma. *Peds in Review*. Nov 2019
- Camargo et al. Managing asthma exacerbations in the Emergency Department: Summary of the NAEPP Expert Panel Report 3 guidelines. *J Allergy Clin Immunol*. Aug 2009
- Seattle Children's Asthma Pathway: https://www.seattlechildrens.org/globalassets/documents/healthcare-professionals/clinical-standard-work/asthma_pathway.pdf
- CHOP Asthma Pathway: <https://www.chop.edu/clinical-pathway/asthma-emergent-care-clinical-pathway>
- Arnold et al. The dilemma of Albuterol dosing in acute asthma exacerbations in pediatrics patients. *Chest*: 2011.
 - Up to 25mg/hr



Audience Question: I prefer Xopenex,
especially if a child needs lots of nebs; it's
better for the heart rate!

- A. Yes
- B. No

A Comparison of Heart Rate Changes Associated with Levalbuterol and Racemic Albuterol in Pediatric Cardiology Patients, *Annals of Pharmacotherapy* - 2013



- Single center review of EMRs
- N=192

• Inclusion criteria:

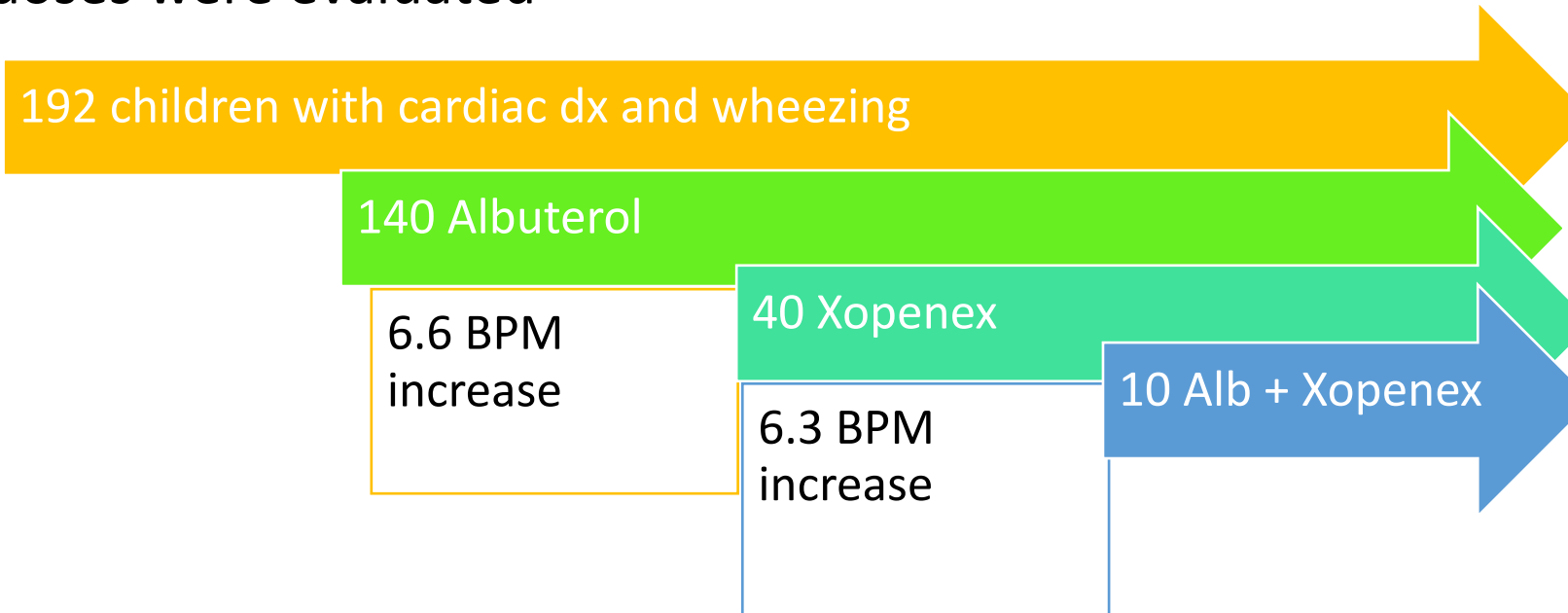
- Received at least 3 doses of levalbuterol and/or racemic albuterol during the study period
- Age younger than 18 years
- Dx of congenital heart disease (CHD), cardiomyopathy, or supraventricular tachycardia

• Exclusion criteria:

- Received a β -blocker or continuous racemic albuterol
- Did not have documented pre- and post dose HRs

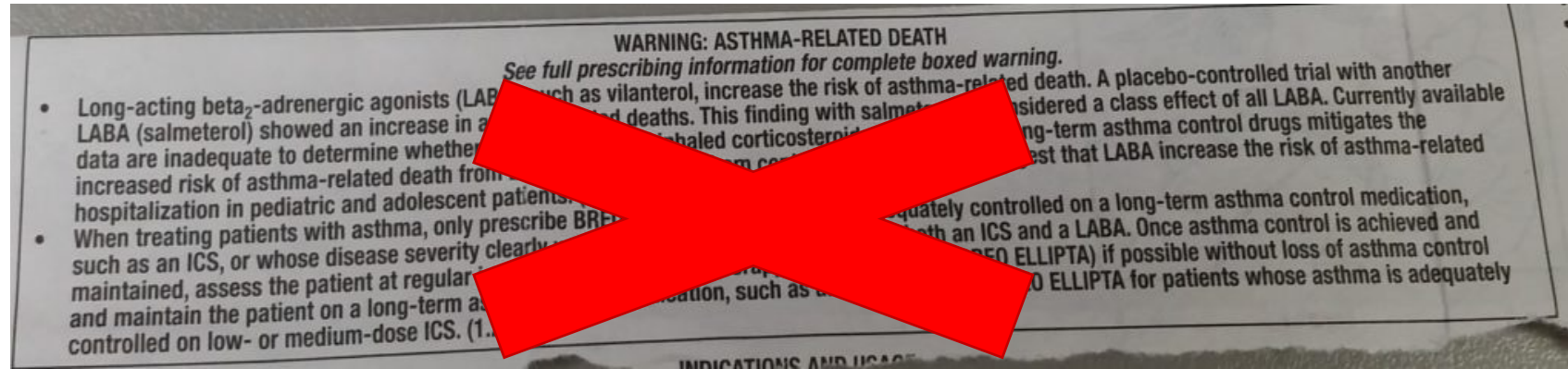
A Comparison of Heart Rate Changes Associated with Levalbuterol and Racemic Albuterol in Pediatric Cardiology Patients, *Annals of Pharmacotherapy* – 2013

- Racemic albuterol and levalbuterol induced an equivalent increase in HR in peds cardiology patients when the first 3 doses were evaluated



**NO DIFFERENCE
between Albuterol
and Xopenex!**

Combined Analysis of Asthma Safety Trials of Long Acting β_2 -Agonists, *NEJM* - 2018



- Initial studies looked at LABA alone: increased risk of death
- 2010: FDA mandated prospective RCTs comparing safety of combo therapy
 - LABA plus an inhaled glucocorticoid (combo therapy) with inhaled glucocorticoid alone
- Independent joint oversight committee - final combined analysis of 4 trials
- N=36,010
- **Combo of LABA and ICS: no increase in serious events**
 - **Improvement in symptoms over ICS alone!**
- Black box warning label removed Dec 2017

Anticholinergics

- Ipratropium bromide (Atrovent): prevents admission when using with Albuterol
- < 30 kg: 0.5 mg X 1
- > 30 kg: 1 mg (2 nebs)

• **No longer recommended in mild exacerbations!**



Patel SJ, Teach SJ. Asthma. Peds in Review. Nov 2019

Audience Question:

4-year-old 20 kg girl presents with near silent chest, diffuse retractions, sats of 87%. Her lips are dusky. She is grunting, unable to cooperate, agitated and crying. Mother states that she has had a cough for 2 days and has been “breathing hard” for the last 8 hours.

What is the first medication you give?

- A. Albuterol
- B. Atrovent
- C. IM/IV steroids
- D. Epinephrine

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Epinephrine

- Insufficient evidence to be recommended universally for severe exacerbations
- Severe or life-threatening exacerbations:
 - Older children - silent chest
 - Younger children - air hungry, hypoxic, and aggressive or disoriented
 - Respiratory arrest
- Epi helps open up airways so that albuterol can get into lower airways more effectively
- Epinephrine 1:1000 (1mg/1ml): 0.01 mg/kg/dose to max 0.5mg IM
 - Dosing is standard and matches dosing for anaphylaxis
- Epi-Pens?

Patel SJ, Teach SJ. Asthma. Peds in Review. Nov 2019

Sellers, WF. Epinephrine auto-injectors for acute asthma, as well as anaphylaxis. Brit Journ General Pract. 2019



Audience Question:
It's time for steroids....

6-year-old boy with moderate asthma exacerbation
who is responding well to albuterol nebs.

What steroid do you give this child?

- A. Dexamethasone
- B. Prednisolone
- C. Other

Oral Steroids – Dexamethasone v. Prednisone

Steroids given in acute exacerbations decrease admissions

Scarfone et al. Pediatrics: Oct 1993

• DEXAMETHASONE

- Longer half-life
- Less vomiting
- 1 or 2 total doses over 1-2 days
 - 1 dose = 5 days Prednisolone
 - Altamimi et al. Peds Em Care, 2006
- Better adherence = better outcomes

• PREDNISONE

- Short half life: BID dosing
- Vomiting
- 5 days
 - Or 3 days?
 - *Chang et al. Med J Aust. 2008*

**NO difference in admission rates, #
Albuterol received, or bounce backs**

Ready for discharge: Inhaled Corticosteroids (ICS) in UC setting?

- HIGH EVIDENCE with **CONDITIONAL RECOMMENDATION**:
 - Children 0-4 years at start of RTI: Add short course ICS + PRN SABA
- HIGH (12 and older) and MODERATE (4-11yrs) EVIDENCE with **STRONG RECOMMENDATION**:
 - **Moderate to severe persistent asthma: High dose ICS with SABA (i.e: Flovent + Albuterol) or same-dose ICS/LABA with SABA (i.e: Qvar + Albuterol)**



2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group

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Croup

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Audience Question:

A 2-year-old patient presents to your office with a barking cough and no stridor at rest.

What is the appropriate choice for oral glucocorticoid therapy?

- A. Prednisolone
- B. Solumedrol
- C. Dexamethasone

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Audience Question:

A 2-year-old patient presents to your office with a barking cough and no stridor at rest.

What is the appropriate dosing option for dexamethasone therapy?

- A. Dexamethasone 0.6mg/kg
- B. Dexamethasone 0.15mg/kg
- C. Dexamethasone 0.3mg/kg

Prednisolone Versus Dexamethasone for Croup, Pediatrics - RCT 2019

- Peds EDs in Australia
- N=1252
- Primary outcome measures:
 - Westley Croup Score (WCS) measure of croup severity
 - Re-attendance for f/u of ongoing symptoms



Prednisolone Versus Dexamethasone for Croup, Pediatrics - RCT 2019

- 3 treatment groups:
 - Dexamethasone 0.6mg/kg (standard/"control" dose) PO
 - Low-dose dexamethasone 0.15mg/kg PO
 - Prednisolone 1mg/kg PO
- **Showed noninferiority of low-dose dexamethasone and prednisolone relative to the standard full dose of dexamethasone**

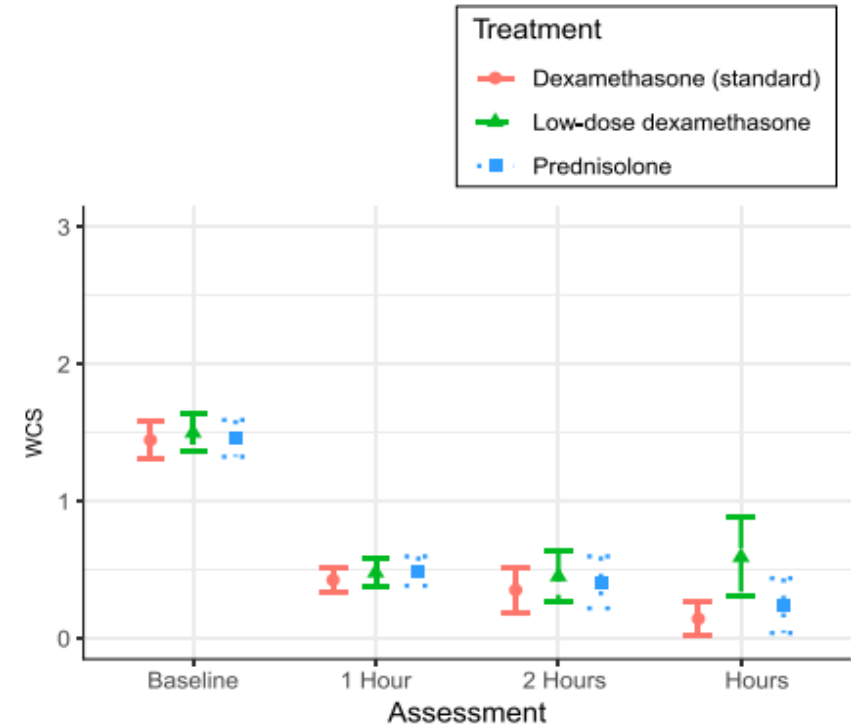


FIGURE 2
Westley Croup Score by time and treatment group. Westley Croup Score, mean and 95% confidence interval by assessment and treatment group; circle and solid line represents dexamethasone, triangle and dashed lined represents low-dose dexamethasone, and square and dotted line represents prednisolone.

Glucocorticoids for Croup in Children – *Cochrane Review* 2023 (update from 2018)

- 45 RCTs, systematic review
- N=5888
- Inclusion Criteria:
 - Must have assessed at least 1 of the following -
 - Primary outcomes: Change in croup score or return visits, (re)admissions to the hospital or both
 - Secondary outcomes: Length of stay in hospital or emergency departments, patient improvement, use of additional treatments, or adverse events
- **Results: Smaller dose of 0.15 mg/kg of dexamethasone may be as effective as std dose of 0.60 mg/kg**
- More RCTs are needed to strengthen evidence for effectiveness of low-dose dexamethasone at 0.15 mg/kg to treat croup

Glucocorticoids for Croup in Children – *Cochrane Review* 2023 (update from 2018)

- Prednisolone v. Dexamethasone

- Little to no difference in reduction of croup score at 2 hr post-baseline score
- Dex probably reduced return visits or (re)admissions for croup by almost 1/2
- Showed 28% reduction in use of supplemental glucocorticoids as additional treatment

Glucocorticoids for Croup in Children – *Cochrane Review* 2023 (update from 2018)

- Dexamethasone 0.15 mg/kg v. 0.60 mg/kg
 - Little to no difference between doses of dex in:
 - Return visits or (re)admissions of children or both
 - Length of stay in the hospital or ED
 - Need for additional treatments i.e: epi, intubation, supplemental glucocorticoids

Pneumonia

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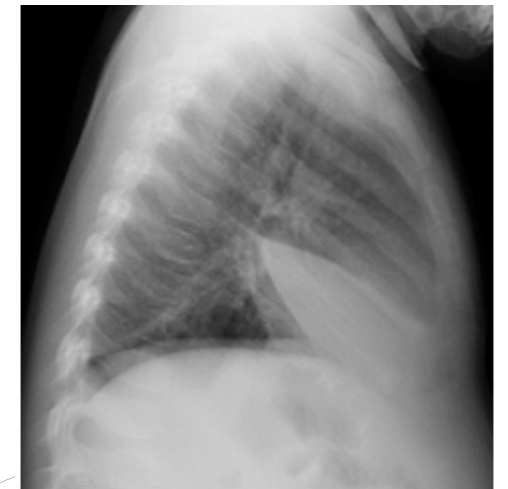
Audience Question:

What is the appropriate duration of antibiotic treatment for pediatric inpatients and outpatients with community acquired pneumonia who are improving?

- A. 5 days
- B. 8 days
- C. 10 days
- D. 14 days

Community Acquired Pneumonia (CAP)

- RCTs for adults with CAP show 5-day course of abx as effective as longer courses
- Few RCTs for peds evaluating short-course abx for CAP
- Current standard: 10-day course of HD Amoxil
- Short Course: 5-day course of HD Amoxil



SAFER (Short-Course Antimicrobial Therapy for Pediatric Respiratory Infections), *JAMA Pediatrics* - RCT 2021

- Peds EDs in Canada
- Ages 6 mos to 10 yrs
- N=281
- Outpatient: 5-day course of HD Amoxil v. 10-day course of HD Amoxil

SAFER (Short-Course Antimicrobial Therapy for Pediatric Respiratory Infections), *JAMA Pediatrics* - RCT 2021

Table 2. Clinical Cure Outcomes

Outcome	Intention-to-treat analysis			Per protocol analysis (adherent to medications)			Strict per protocol analysis (adherent to medications and consolidation on radiograph)		
	Patient group ^a			Patient group ^a			Patient group ^a		
	Intervention (n = 140)	Control (n = 141)	RD (97.5% 1-sided CL)	Intervention (n = 122)	Control (n = 114)	RD (97.5% 1-sided CL)	Intervention (n = 86)	Control (n = 87)	RD (97.5% 1-sided CL)
Clinical cure (primary)	108 (85.7)	106 (84.1)	0.023 (-0.061 to ∞)	101 (88.6)	99 (90.8)	-0.016 (-0.087 to ∞)	73 (89.0)	74 (89.2)	-0.011 (-0.096 to ∞)
Missing data, No.	14	15	29	8	5	13	4	4	8
Clinical cure not requiring additional intervention (secondary)	116 (93.5)	113 (90.4)	0.028 (-0.038 to ∞)	107 (95.5)	104 (95.4)	-0.006 (-0.055 to ∞)	76 (95.0)	78 (94.0)	-0.004 (-0.071 to ∞)
Missing data, No.	16	16	32	10	5	15	6	4	10

Abbreviations: CL, confidence limit; RD, risk difference.

^a Unless otherwise indicated, data are expressed as number (percentage) of patients.

• Short-course treatment was found to be statistically noninferior



SCOUT-CAP (Short- vs Standard-Course Outpatient Antibiotic Therapy for CAP in Children), *JAMA Pediatrics* - RCT 2022

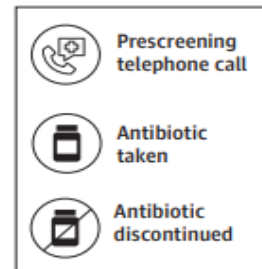
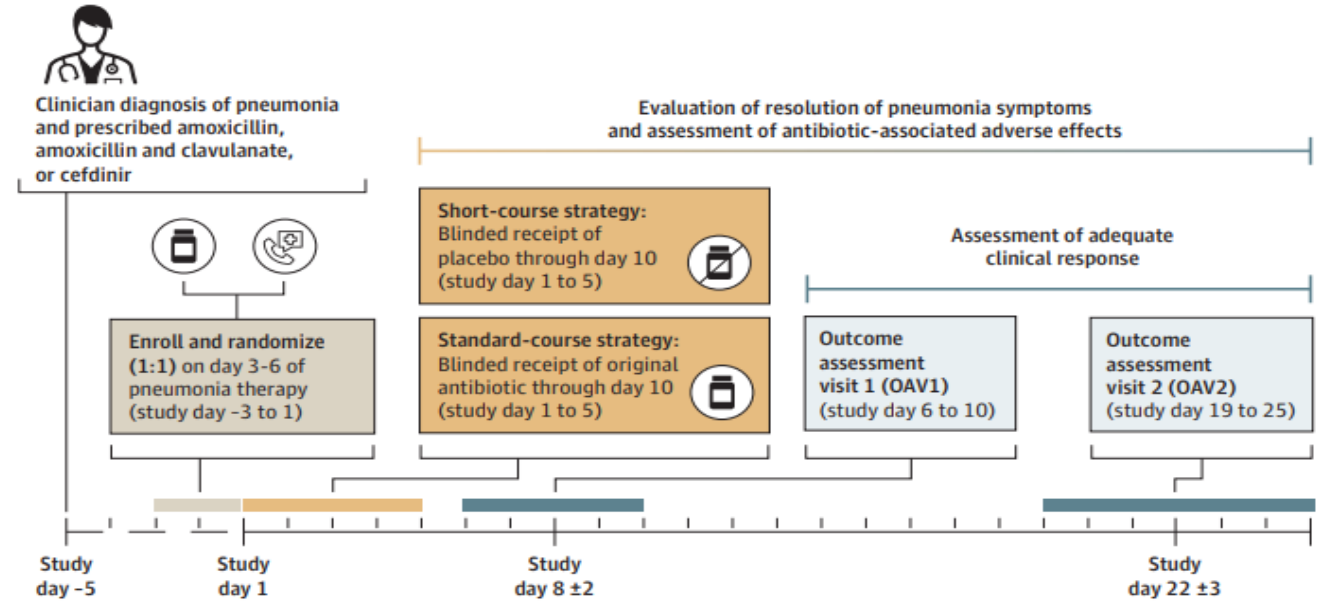
- Multicenter study, Tennessee
- Ages 6 mos to 71 mos (6yrs)
- N=380
- Primary endpoint: End-of-treatment response adjusted for duration of antibiotic risk (RADAR)
- Outpatient: 5-day course of HD Amoxil v. 10-day course of HD Amoxil

SCOUT-CAP (Short- vs Standard-Course Outpatient Antibiotic Therapy for CAP in Children), *JAMA Pediatrics* - RCT 2022

- Inclusion criteria:
 - Otherwise healthy children diagnosed with uncomplicated CAP in an outpatient clinic, UC, ED and treated with Amox, Amox-Clav or Cefdinir
 - Enrolled on days 3 to 6 of initially prescribed therapy
- Exclusion criteria: (remember enrolled on days 3-6 of tx)
 - Fever within 24hrs of presentation
 - Tachypnea
 - Severe cough

SCOUT-CAP (Short- vs Standard-Course Outpatient Antibiotic Therapy for CAP in Children), *JAMA Pediatrics* - RCT 2022

- DOOR components:
 - Adequate clinical response
 - Resolution of symptoms
 - Presence and severity of abx-associated adverse effects
 - Rank 1 = best possible outcome
 - Rank 8 = worst possible outcome



Assessments at OAV1 and OAV2			
Rank	Adequate clinical response	Resolution of pneumonia symptoms	Maximal antibiotic-associated adverse effects
1	Yes	Resolved	None
2	Yes	Resolved	Mild
3	Yes	Resolved	Moderate
4	Yes	Resolved	Severe
5	Yes	Persistent symptoms	Any
6	No, ED/clinic visit only	Any	Any
7	No, hospitalization	Any	Any
8	Death from any cause	Any	Any

SCOUT-CAP (Short- vs Standard-Course Outpatient Antibiotic Therapy for CAP in Children), *JAMA Pediatrics* - RCT 2022

- **5-day abx course superior to a 10-day course**
- Similar:
 - Clinical response
 - Resolution of symptoms
 - Abx-associated adverse effects

How you can drive change:

- Do not fear albuterol! Most institutions using up to 20mg/hr
- Consider low dose dexamethasone in croup management
- Consider 5-day antibiotic course in CAP

DRIVING **CHANGE2023**

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Not likely at all Neutral Extremely likely

0 1 2 3 4 5 6 7 8 9 10

What did you find most valuable about this **content**?

What would have made this **content** better?

References

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Thank you!

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