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MEDICAL CENTER

Gadgets and Gizmos

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Disclosures

- No conflicts of interest to disclose
- I'm not a medical device engineer
- Health services researcher, Clinical outcomes expert, and General Pediatrician...
- ... *with a "think outside the box" mindset*

Thanks to Barry Lachman, *MD, MPH, FAAP*



CME Learning Objective

- Discuss asthma education and demonstrate common asthma equipment and devices

Session Learning Objectives



- Explore the trends in inhaler device design
- Review the medical evidence regarding use of nebulizers versus spacers & chambers
- Discuss the role of fractionated exhaled nitric oxide (FeNO) in asthma management
- Learn how remote electronic monitoring can empower both providers and recipients of asthma care – ***Cause for optimism***



Expert Panel Report (EPR) No. 3

August 28, 2007

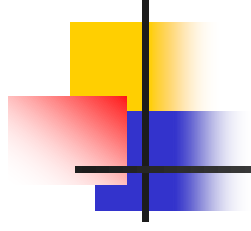
Section 3, The Four Components of Asthma Management

SECTION 3, THE FOUR COMPONENTS OF ASTHMA MANAGEMENT

Introduction

The Expert Panel Reports presenting clinical practice guidelines for the diagnosis and management of asthma have organized recommendations for asthma care around four components considered essential to effective asthma management:

- Measures of assessment and monitoring, obtained by objective tests, physical examination, patient history and patient report, to diagnose and assess the characteristics and severity of asthma and to monitor whether asthma control is achieved and maintained
- Education for a partnership in asthma care
- Control of environmental factors and comorbid conditions that affect asthma
- Pharmacologic therapy



Asthma Control Questionnaires

Childhood Asthma Control Test for children 4 to 11 years

Know your score.

Parent or Guardian: The Childhood Asthma Control Test* is a way to help your child's healthcare provider determine if your child's asthma symptoms are well controlled. Take this test with your child (ages 4 to 11). Share the results with your child's healthcare provider.

Step 1: Have your child answer the first four questions (1 to 4). If your child needs help, you may help, but let your child choose the answer.

Step 2: Answer the last three questions (5 to 7) on your own. Don't let your child's answers influence yours. There are no right or wrong answers.

Step 3: Write the number of each answer in the score box to the right.

Step 4: Add up each score box for the total.

Step 5: Take the COMPLETED test to your child's healthcare provider to talk about your child's total score.

19
or less

If your child's score is 19 or less, your child's asthma symptoms may not be as well controlled as they could be. No matter what the score, bring this test to your child's healthcare provider to talk about your child's results.

Have your child complete these questions.

1. How is your asthma today?

 5 Very bad	 1 Bad	 2 Good	 3 Very good
--	---	--	---

2. How much of a problem is your asthma when you run, exercise or play sports?

 0 It's a big problem, I can't do what I want to do.	 1 It's a problem and I don't like it.	 2 It's a little problem but it's okay.	 3 It's not a problem.
---	---	--	---

3. Do you cough because of your asthma?

 0 Yes, all of the time.	 1 Yes, most of the time.	 2 Yes, some of the time.	 3 No, none of the time.
---	--	--	---

4. Do you wake up during the night because of your asthma?

 0 Yes, all of the time.	 1 Yes, most of the time.	 2 Yes, some of the time.	 3 No, none of the time.
---	--	--	---

Please complete the following questions on your own.

5. During the last 4 weeks, how many days did your child have any daytime asthma symptoms?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday
-----------------	---------------	----------------	-----------------	-----------------	---------------

6. During the last 4 weeks, how many days did your child wheeze during the day because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday
-----------------	---------------	----------------	-----------------	-----------------	---------------

7. During the last 4 weeks, how many days did your child wake up during the night because of asthma?

5 Not at all	4 1-3 days	3 4-10 days	2 11-18 days	1 19-24 days	0 Everyday
-----------------	---------------	----------------	-----------------	-----------------	---------------

*The Childhood Asthma Control Test was developed by GSK.

This material was developed by GSK.



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All rights reserved. Produced in USA. 5010490 December 2014

SCORE

TOTAL

Name: _____

Today's Date: _____

ASTHMA CONTROL TEST™

Know your score.

The Asthma Control Test™ provides a numerical score to help you and your healthcare provider determine if your asthma symptoms are well controlled.

Take this test if you are 12 years or older. Share the score with your healthcare provider.

Step 1: Write the number of each answer in the score box provided.

Step 2: Add up each score box for the total.

Step 3: Take the completed test to your healthcare provider to talk about your score.

IF YOUR SCORE IS 19 OR LESS, Your asthma symptoms may not be as well controlled as they could be.

No matter what the score, bring this test to your healthcare provider to talk about the results.

NOTE: If your score is 15 or less, your asthma may be very poorly controlled. Please contact your healthcare provider right away. There may be more you and your healthcare provider could do to help control your asthma symptoms.

- | | | | | | | SCORE |
|--|--------------------------|---------------------------|--------------------------|---------------------------|--|-------|
| 1. In the <u>past 4 weeks</u> , how much of the time did your <u>asthma</u> keep you from getting as much done at work, school or at home? | | | | | | |
| All of the time [1] | Most of the time [2] | Some of the time [3] | A little of the time [4] | None of the time [5] | | |
| 2. During the <u>past 4 weeks</u> , how often have you had shortness of breath? | | | | | | |
| More than Once a day [1] | Once a day [2] | 3 to 6 times a week [3] | Once or twice a week [4] | Not at all [5] | | |
| 3. During the <u>past 4 weeks</u> , how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning? | | | | | | |
| 4 or more nights a week [1] | 2 to 3 nights a week [2] | Once a week [3] | Once or twice [4] | Not at all [5] | | |
| 4. During the <u>past 4 weeks</u> , how often have you used your rescue inhaler or nebulizer medication (such as albuterol)? | | | | | | |
| 3 or more times per day [1] | 1 to 2 times per day [2] | 2 or 3 times per week [3] | Once a week or less [4] | Not at all [5] | | |
| 5. How would you rate your asthma control during the past 4 weeks? | | | | | | |
| Not Controlled at All [1] | Poorly Controlled [2] | Somewhat Controlled [3] | Well Controlled [4] | Completely Controlled [5] | | |

TOTAL:

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Asthma Control Test is a trademark of QualityMetric Incorporated.

This material was developed by GSK.





Medication Inhalers

Types of Inhalers



- 1. **Hydrofluoroalkane inhalers** or **HFA** [∩] (formerly metered dose inhalers or MDI[∫]) – ***Some used with Spacers or Valved Holding Chambers (VHCs)***
- 2. **Dry Powder Inhalers (DPI)** – not for children aged < 5-6 years
- 3. **Soft Mist Inhalers (SMI)** – only ≥5 years of age

[∩] Are either non-breath activated (majority) or breath-activated (more expensive!)

[∫] Metered dose inhalers with chlorofluorocarbons (CFCs) have been phased out due to concerns about damage to the environment.

Respiratory Inhalers

At a Glance 2017

Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.



AllergyAsthmaNetwork.org
800.878.4403

Short-acting beta₂-agonist bronchodilators

ProAir®
HFA
albuterol sulfate
123 A



ProAir®
RespiClick
albuterol sulfate
inhalation powder
123 A



Proventil®
HFA
albuterol sulfate
A



Ventolin®
HFA
albuterol sulfate
123 A



Xopenex
HFA®
levosalbutamol tartrate
A



Long-acting beta₂-agonist bronchodilators

Arcapta™
Neohaler™
indacaterol
inhalation powder
C



Serevent®
Diskus®
salmeterol xinafoate
inhalation powder
123 A C



Striverdi®
Respimat®
olodaterol
hydrochloride
123 C



Inhaled corticosteroids

Aerospan®
80 mcg
fluticasone
★ A



Alvesco® HFA
80 mcg, 160 mcg
ciclesonide
123 A



Arnuity® Ellipta®
100 mcg, 200 mcg
fluticasone furoate
inhalation powder
123 A



Asmanex® HFA
mometasone furoate
123 A



Asmanex®
Twisthaler®
110 mcg, 220 mcg
mometasone furoate
inhalation powder
123 A



Flovent® Diskus®
50 mcg, 100 mcg,
250 mcg
fluticasone propionate
inhalation powder
123 A



Flovent® HFA
44 mcg, 110 mcg, 220 mcg
fluticasone propionate
123 A



Pulmicort
Flexhaler®
90 mcg, 180 mcg
budesonide inhalation powder
123 A



QVAR® (HFA)
40 mcg, 80 mcg
beclomethasone dipropionate
123 A



Combination inhaled corticosteroid and long-acting beta₂-agonist

Advair
Diskus®
100/50, 250/50,
500/50
fluticasone propionate
and salmeterol
inhalation powder
123 A C



Advair® HFA
45/21, 115/21,
230/21
fluticasone propionate
and salmeterol
xinafoate
123 A



Breo® Ellipta®
100/25 mcg, 200/25 mcg
fluticasone furoate
and vilanterol
inhalation powder
123 A C



Dulera®
100/5, 200/5
mometasone furoate
and formoterol fumarate
dihydrate
123 A



Symbicort® (HFA)
80/4.5, 160/4.5
budesonide and
formoterol fumarate
dihydrate
123 A C



Anoro® Ellipta®
62.5 mcg/25 mcg
umeclidinium and vilanterol
inhalation powder
123 C



Bevespi
Aerosphere®
9 mcg/4.8 mcg
glycopyrrolate and
formoterol fumarate
inhalation aerosol
123 C



Stiolto™
Respimat®
2.5 mcg/2.5 mcg
tiotropium bromide
and olodaterol
123 C



Utibron™
Neohaler®
27.5 mcg/15.6 mcg
indacaterol and
glycopyrrolate
inhalation powder
C



Anticholinergics

Short-acting

Atrovent® HFA
ipratropium
bromide
123 C



Long-acting

Seebri™ Neohaler®
glycopyrrolate
inhalation powder
C



Incruse®
Ellipta®
umeclidinium
inhalation powder
123 C



Spiriva®
HandiHaler®
tiotropium bromide
inhalation powder
C



Spiriva®
Respimat®
tiotropium
bromide
123 A C



Tudorza™
Pressair™
aclidinium bromide
inhalation powder
123 C



Combination inhaled anticholinergic and short-acting beta₂-agonist

Combivent®
Respimat®
ipratropium bromide
and albuterol
123 C



FDA OKs *QVAR RediHaler* for Asthma in Children Aged 4+

Megan Brooks

DISCLOSURES | August 11, 2017



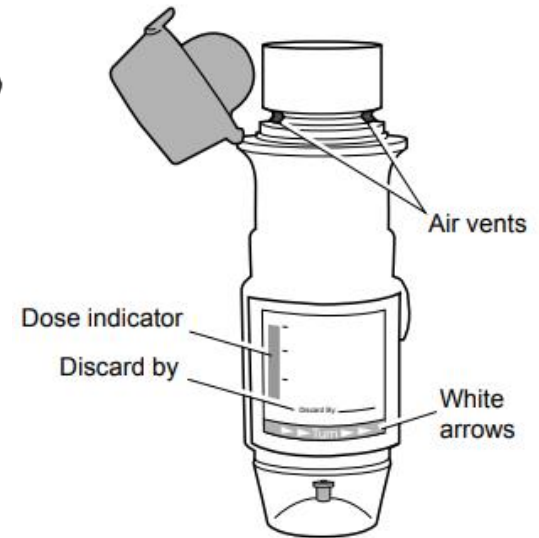
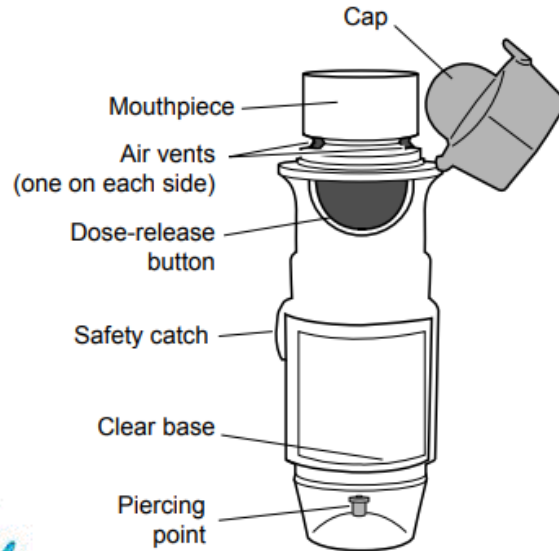
QVAR RediHaler. *Photo courtesy of Teva Pharmaceuticals, Inc.*

Arnuity's Ellipta (fluticasone furoate) Inhaler



Indicated for once-daily maintenance treatment of asthma as prophylactic therapy in children aged ≥ 5 years

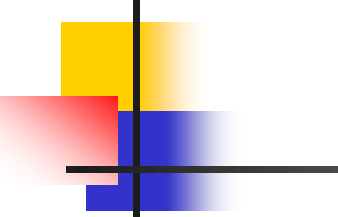
Respimat® Soft Mist™ Inhalers (SMI)



Aqua (2.5 mcg/puff)
2 puffs, once a day

Blue (1.25 mcg/puff)
2 puffs, once a day

Suitable VHC with face mask recommended below 5 years of age. Without VHC, Respimat® may be used by children aged 5 years and above.



In Vitro Determination of Respimat[®] Dose Delivery in Children: An Evaluation Based on Inhalation Flow Profiles and Mouth–Throat Models

Deborah Bickmann,¹ Wolfgang Kamin, MD, PhD,² Ashish Sharma, PhD, RPh,³ Herbert Wachtel, PhD,¹
Petra Moroni-Zentgraf, MD,¹ and Stefan Zielen, MD, PhD⁴

Abstract

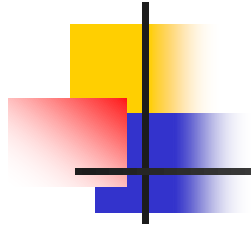
Background: Aerosol therapy in young children can be difficult. A realistic model based on handling studies and *in vitro* investigations can complement clinical deposition studies and be used to enable dose-to-the-lung (DTL) predictions.

Methods: Predictions on dose delivery to the lung were based on (1) representative inhalation flow profiles from children enrolled in a Respimat[®] handling study, (2) *in vitro* measurement of the fine-particle DTL using mouth–throat models derived from nuclear magnetic resonance/computed tomography (NMR/CT) scans of children, and (3) a mathematical model to predict the tiotropium DTL. Accuracy of the prediction was confirmed using pharmacokinetic (PK) data from children with cystic fibrosis enrolled in a phase 3 clinical trial of tiotropium Respimat with valved holding chamber (VHC).

Results: Representative inhalation flow profiles for each age group were obtained from 56 children who successfully inhaled a volume >0.15 L from the Respimat with VHC. Average dimensions of the mouth–throat region for 38 children aged 1–<2 years, 2–<3 years, 3–<4 years, and 4–<5 years were determined from NMR/CT scans. The DTL from the Respimat plus VHC were determined by *in vitro* measurement and were $5.1 \pm 1.1\%$, $15.6 \pm 1.4\%$, $17.9 \pm 1.5\%$, and $37.1 \pm 1.8\%$ of the delivered dose for child models 0–<2 years, 2–<3 years, 3–<4 years, and 4–<5 years, respectively. This provides a possible explanation for the age dependence of clinical PK data obtained from the phase 3 tiotropium trial. Calculated *in vitro* DTL per body mass ($\mu\text{g}/\text{kg}$ [$\pm\text{SD}$]) were 0.031 ± 0.014 , 0.066 ± 0.031 , 0.058 ± 0.024 , and 0.059 ± 0.029 , respectively, compared to 0.046 in adults. Therefore, efficacy of the treatment was not negatively impacted in spite of the seemingly low percentages of the DTL.

Conclusions: We conclude that the combination of real-life inhalation profiles with respective mouth–throat models and *in vitro* determination of delivered DTL is a good predictor of the drug delivery to children via the Respimat with VHC. The data provided can be used to support data from appropriate clinical trials.

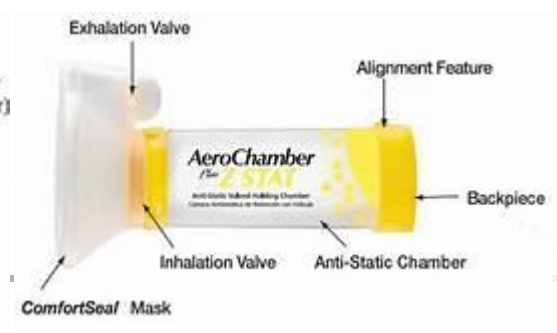
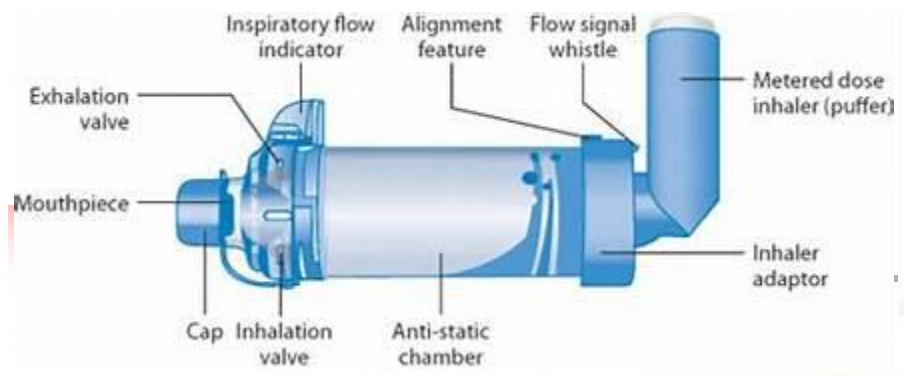
Key words: children, fine particle-fraction, inhalation breathing pattern, inspiratory flow, lung deposition, Respimat[®] Soft Mist[™] Inhaler



Spacers & Valved Holding Chambers

Various Shapes & Styles of Spacers





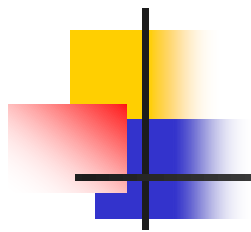
Correct Use of HFA Inhaler with a Spacer

<https://youtu.be/BbONuRXJdr0>

Role of a Valved Holding Chamber (VHC)



<https://youtu.be/Trqc8shfSGA>



Nebulizers



Innospire Go Portable Mesh Nebulizer



Sami the Seal Nebulizer Compressor

NEW!



Innospire Go Portable Mesh Nebulizer (Damaged Box)

NEW!



Omron Mesh Nebulizer NE-U100



Jo Jo the Jelly Fish Nebulizer System



Aerial™ Express Compressor Nebulizer



Medquip Panda Nebulizer System

NEW!



Clown Fish Pediatric Compressor Nebulizer



Checker Nebulizer (Yellow) - Kit



Medquip Fire Engine Nebulizer System

BEST PEDIATRIC



PARI TREK S Compact Compressor Combination Pack



PARI Vios - Pediatric

NEW!



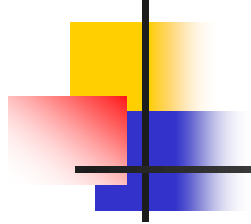
Buddy the Dog Pediatric Nebulizer Compressor



Drive Beagle Pediatric Nebulizer System

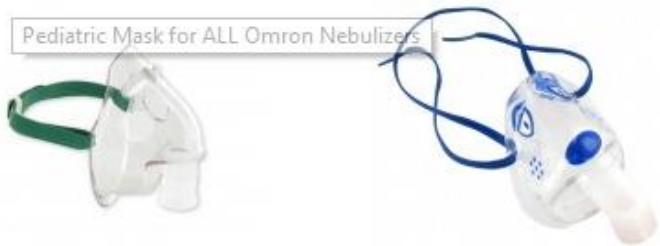


Neb-u-Tyke Train Nebulizer System



Face Masks

Pediatric Mask for ALL Omron Nebulizers



Pediatric Mask for ALL Omron Nebulizers



Pediatric Dragon Mask



Eden the Elephant Pediatric Mask



Bubbles the Fish Pediatric Aerosol Mask



Child Mask for ALL Standard Nebulizer Kits



PARI Baby Conversion Kit



DeVilbiss Pediatric Mask



Turtle Infant Respiratory Mask



Tucker the Turtle Pediatric Mask



PARI Chloe Ladybug Infant Mask for PARI Vortex Holding Chamber



PARI Felix Frog Child Mask for PARI Vortex Holding Chamber



Medquip Pedi-Neb Pacifier



MicroElite Pediatric Mask



PARI Baby Reusable Nebulizer Set

PHARMACOTHERAPY

Spacers versus nebulizers in treatment of acute asthma – a prospective randomized study in preschool children

Niki Mitselou, MD¹, Gunilla Hedlin, MD, PhD², and Carl-Axel Hederos, MD, PhD³

¹Department of Pediatrics, Örebro University Hospital, Örebro, Sweden, ²Department of Women's and Children's Health and Centre for Allergy Research, Karolinska Institutet, Astrid Lindgren Children's Hospital, Stockholm, Sweden, and ³Department of Pediatrics, Karlstad Central Hospital, Karlstad, Sweden

Abstract

Objective: To compare administration of bronchodilators by nebulizers with delivery by metered dose inhalers (MDIs) with spacers and to evaluate the clinical effect of the treatment of acute asthma in preschool children. **Methods:** A prospective randomized clinical trial in a pediatric emergency department (PED). Preschool children who were admitted for virus induced wheezing or acute asthma exacerbation were randomly allocated to receive bronchodilator treatment by nebulizer or by metered dose inhaler. The accompanying parents completed a questionnaire. **Results:** The length of stay in the PED and the hospitalization rate were similar and no difference was seen in the parents' view of ease of use and device acceptance. Baseline data were similar for both groups apart from the family history of asthma and atopic disease that was greater in the nebulizer group. No significant differences were seen in heart rate, respiratory rate and oxygen saturation at baseline and after the treatment. According to the parents 40% of the participants had asthma diagnosis though up to 66% had some kind of asthma medication. **Conclusions:** Our data suggests that MDIs with spacers are at least as effective as nebulizers in the delivery of beta agonists to treat preschool children with virus induced wheezing or acute exacerbations of asthma in the PED. Parents may underestimate the gravity of their children's asthma. It is mandatory to provide adequate information to the staff and parents in order to treat pediatric acute asthma successfully.

Keywords

Emergency department, pediatric, information, wheezing, bronchodilators, metered dose inhalers, hospitalization rate

History

Received 11 February 2016

Revised 24 March 2016

Accepted 26 April 2016



Primary Outcomes

Table 5. Length of stay, hospitalization rate and how the parents experienced their child's treatment.

	Group A (Nebulizer) N = 53	Group B (Spacer) N = 45
Length of stay (minutes) \pm SD	153.33 \pm 80.39	153.60 \pm 97.57
Admission rate: n (%)	6 (11.3%)	7 (15.6%)
Parents' opinion on the acute asthma treatment: mean \pm SD	3.46 \pm 2.69	3.65 \pm 3.04



Secondary Outcomes

Table 2. Heart rate, respiratory rate and saturation at baseline and after the last treatment.

		Group A (Nebulizer) N = 53	Group B (Spacer) N = 45
Heart rate (beats/min): mean \pm SD	at baseline	142.21 \pm 21.68	139.52 \pm 20.14
	after treatment	155.89 \pm 22.63	148.35 \pm 17.77
	difference	12.96 \pm 17.63	6.23 \pm 25.75
Respiratory rate (breaths/min): mean \pm SD	at baseline	40.86 \pm 11.16	39.92 \pm 11.03
	after treatment	36.71 \pm 10.95	35.75 \pm 10.69
	difference	-4.69 \pm 9.97	-3.52 \pm 10.00
SaO ₂ (saturation %): mean \pm SD	at baseline	96.00 \pm 2.64	95.98 \pm 2.44
	after treatment	96.50 \pm 2.21	96.52 \pm 2.26
	difference	0.63 \pm 2.66	0.50 \pm 2.65

Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma (Review)



**Cochrane
Library**

Cochrane Database of Systematic Reviews

Cates CJ, Welsh EJ, Rowe BH

www.cochranelibrary.com

ABSTRACT

Background

In acute asthma inhaled beta₂-agonists are often administered by nebuliser to relieve bronchospasm, but some have argued that metered-dose inhalers with a holding chamber (spacer) can be equally effective. Nebulisers require a power source and need regular maintenance, and are more expensive in the community setting.

Objectives

To assess the effects of holding chambers (spacers) compared to nebulisers for the delivery of beta₂-agonists for acute asthma.

Search methods

We searched the Cochrane Airways Group Trial Register and reference lists of articles. We contacted the authors of studies to identify additional trials. Date of last search: February 2013.

Selection criteria

Randomised trials in adults and children (from two years of age) with asthma, where spacer beta₂-agonist delivery was compared with wet nebulisation.

Data collection and analysis

Two review authors independently applied study inclusion criteria (one review author for the first version of the review), extracted the data and assessed risks of bias. Missing data were obtained from the authors or estimated. Results are reported with 95% confidence intervals (CIs).

Main results

This review includes a total of 1897 children and 729 adults in 39 trials. Thirty-three trials were conducted in the emergency room and equivalent community settings, and six trials were on inpatients with acute asthma (207 children and 28 adults). The method of delivery of beta₂-agonist did not show a significant difference in hospital admission rates. In adults, the risk ratio (RR) of admission for spacer versus nebuliser was 0.94 (95% CI 0.61 to 1.43). The risk ratio for children was 0.71 (95% CI 0.47 to 1.08, moderate

Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma (Review)
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WILEY

Citation: Cates CJ, Welsh EJ, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Cochrane Database of Systematic Reviews 2013, Issue 9. Art. No.: CD000052. DOI: 10.1002/14651858.CD000052.pub3. Copyright © 2014 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanations]

Multiple treatment of beta ₂ -agonist via spacer (chamber) compared to nebuliser for children with acute asthma						
Patient or population: children with acute asthma Settings: Community or Emergency Department Intervention: Multiple treatments with beta ₂ -agonist via spacer (chamber) Comparison: Multiple treatments with beta ₂ -agonist via nebuliser						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Nebuliser	Multiple treatment of beta ₂ -agonist via spacer (chamber)				
Hospital admission	110 per 1000	78 per 1000 (52 to 119)	RR 0.71 (0.47 to 1.08)	757 (9 studies)	⊕⊕○○ low ^{1,2}	Large increases in the proportion of children admitted to hospital on spacer in comparison to nebuliser are ruled out by this 95% confidence interval
Duration in emergency department (minutes)	The mean duration in emergency department (minutes) in the control groups was 103 minutes	The mean duration in emergency department (minutes) in the intervention groups was 33 minutes shorter (43 minutes shorter to 24 minutes shorter)		398 (3 studies)	⊕⊕⊕○ moderate ¹	There was a consistent direction of shortening of time in ED in all 3 studies, and although the size of this effect varied between studies ($I^2 = 66\%$), we felt that the mean difference was important in all studies

Final rise in FEV ₁ (% predicted)	The mean final rise in FEV ₁ (% predicted) in the control groups was 27% predicted at baseline	The mean final rise in FEV ₁ (% predicted) in the intervention groups was 0.92% higher (4.96% lower to 6.79% higher)		48 (2 studies)	⊕⊕○○ low ^{1,2}	
Rise in pulse rate (% baseline)	The mean rise in pulse rate (% baseline) in the control groups was 7% rise from baseline	The mean rise in pulse rate (% baseline) in the intervention groups was 5.62% lower (7.52% to 3.72% lower)		670 (9 studies)	⊕⊕⊕○ moderate ¹	
Number of participants developing tremor	142 per 1000	91 per 1000 (62 to 135)	RR 0.64 (0.44 to 0.95)	254 (4 studies)	⊕⊕⊕○ moderate ¹	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

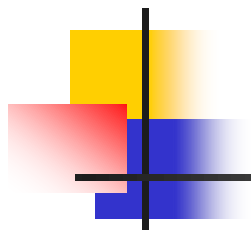
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹ Mostly open label studies

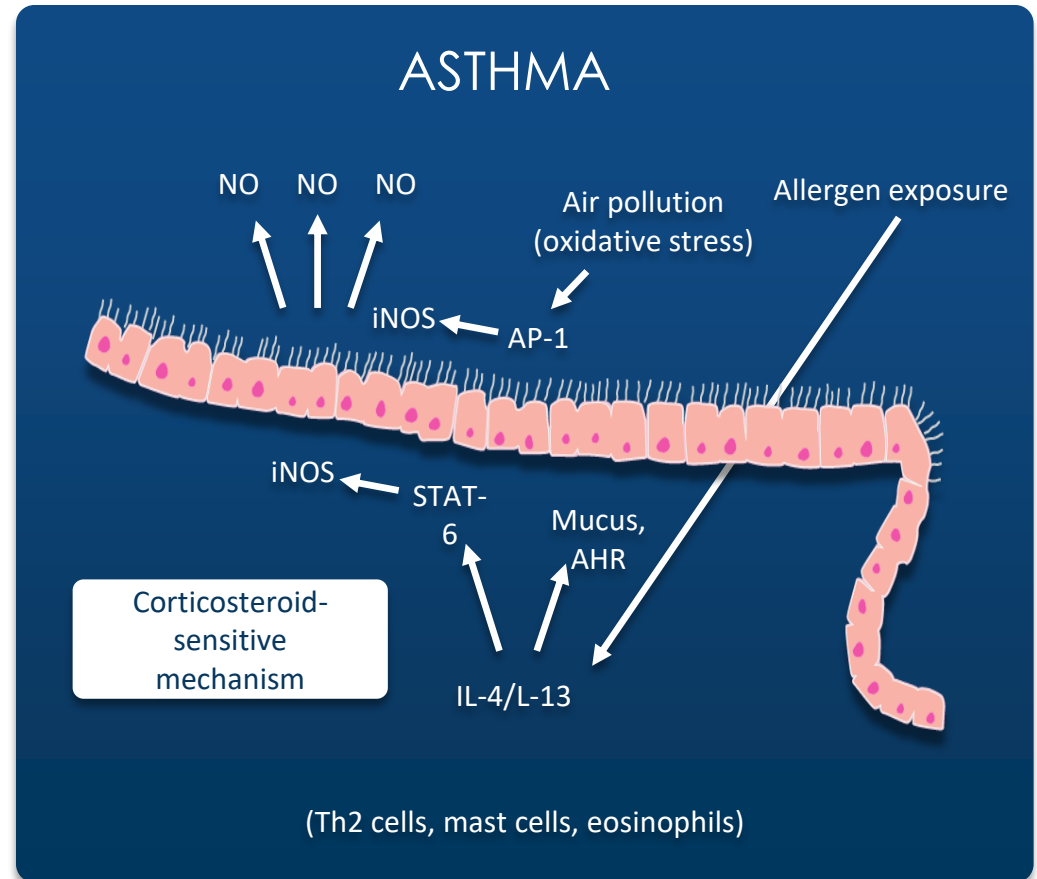
² Wide confidence intervals



Fractionated Exhaled Nitric Oxide (FeNO)

Exhaled NO Is a Marker of Airway Inflammation¹⁻³

- NO is an endogenous regulatory molecule¹
- Synthesis regulated by family of enzymes (NOS)¹
- iNOS-derived NO predominantly produced in bronchial wall epithelial cells^{2,3}
- Exhaled NO levels increase during allergic inflammation and often correlate with eosinophilic inflammation^{2,3}



AHR, airway hyperresponsiveness; AP, activator protein; IL, interleukin; iNOS, inducible nitric oxide synthase; NO, nitric oxide; NOS, nitric oxide synthase; STAT, signal transducer and activator of transcription.

1. Yates. *Immunol Cell Biol.* 2001;79:178-190. 2. Alving and Malinovschi. *Eur Respir Mon.* 2010;49:1-31. 3. Mummadi and Hahn. *Chest.* 2016;149:1340-1344.

The NIOX VERO[®] Portable Device

- Currently the only available point-of-care device to measure FeNO
- Appropriate for patients ≥ 7 years of age
- Easy-to-follow, on-screen guidance
 - 10 seconds of active patient participation with a moderate exhalation (50 mL/sec)
 - Results available in approximately 1 minute



Empty lungs



Inhale deeply
through
disposable filter



Exhale through
disposable filter
for **10 seconds**

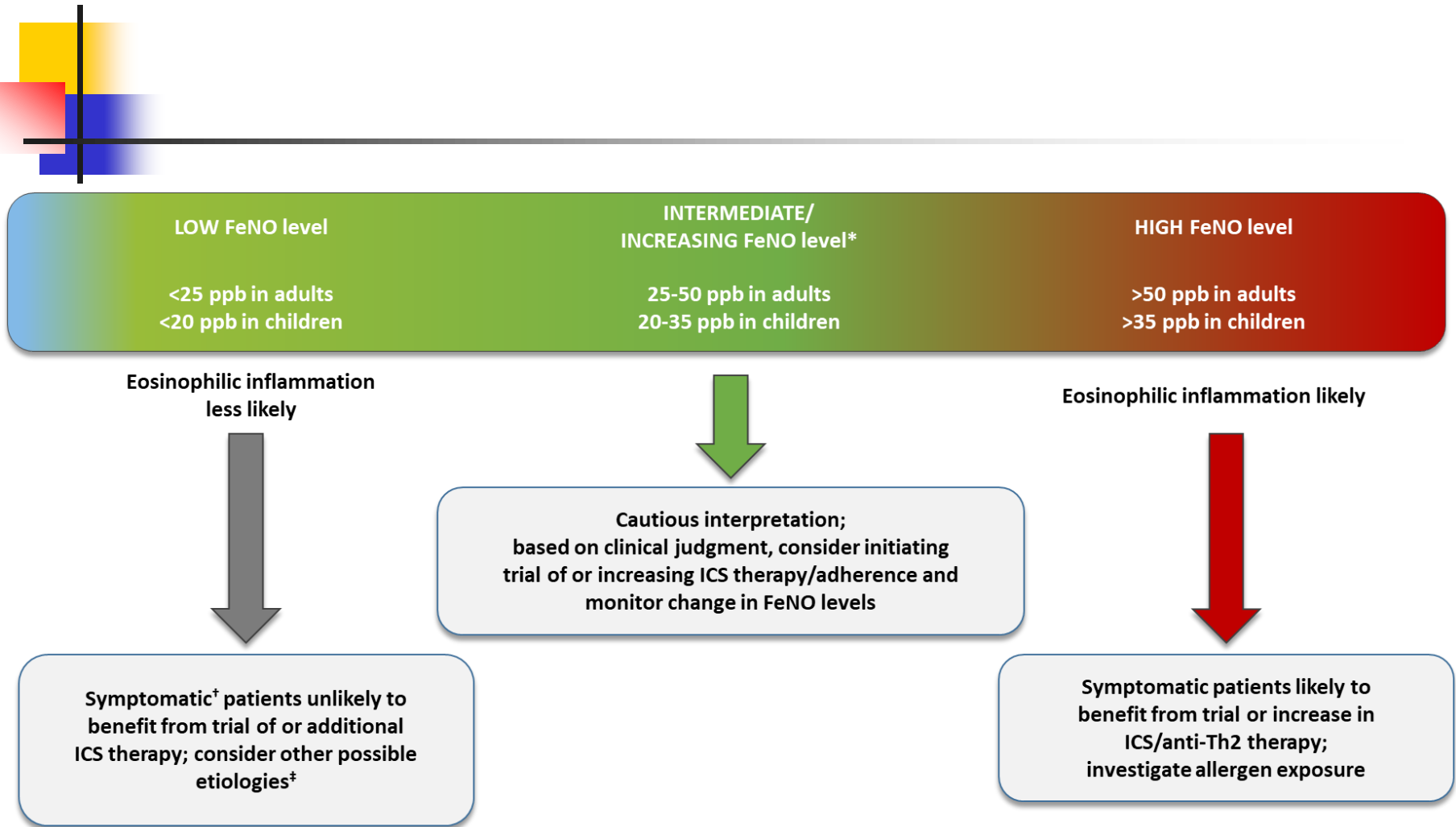


View results on
screen in
approximately
60 seconds

- Unlike PFTs, a result cannot be affected by patient effort
- If the patient exhales outside of range (high/low), no result is delivered, and the test can quickly be restarted



FeNO Interpretation¹



FeNO, fractional exhaled nitric oxide; GERD, gastroesophageal reflux disease.

*Increasing defined as >40% increase from previous stable FeNO level. [†]Chronic cough and/or wheeze and/or shortness of breath for >6 weeks.

[‡]For example, rhinosinusitis, bronchiectasis, primary ciliary dyskinesia, anxiety-hyperventilation, cardiac disease, GERD, or vocal cord dysfunction.

1. Dweik et al. *Am J Respir Crit Care Med.* 2011;184:602-615.

Exhaled nitric oxide levels to guide treatment for children with asthma (Review)

ABSTRACT

Background

Asthma guidelines aim to guide health practitioners to optimise treatment for patients to minimise symptoms, improve or maintain good lung function, and prevent acute exacerbations. The principle of asthma guidelines is based on a step-up or step-down regimen of asthma medications to maximise health using minimum doses. Fractional exhaled nitric oxide (FeNO) is a marker of eosinophilic inflammation and tailoring asthma medications in accordance to airway eosinophilic levels may improve asthma outcomes such as indices of control or reduce exacerbations, or both.

Objectives

To evaluate the efficacy of tailoring asthma interventions based on fractional exhaled nitric oxide (FeNO), in comparison to not using FeNO, that is, management based on clinical symptoms (with or without spirometry/peak flow) or asthma guidelines (or both), for asthma-related outcomes in children.

Search methods

We searched the Cochrane Airways Group Specialised Register of Trials, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase and reference lists of articles. The last searches were in June 2016.

Selection criteria

All randomised controlled trials (RCTs) comparing adjustment of asthma medications based on FeNO levels compared to those not using FeNO, that is, management based on clinical symptoms or asthma guidelines (or both) involving children.

Data collection and analysis

We reviewed results of searches against predetermined criteria for inclusion. Two review authors independently selected relevant studies, assessed trial quality and extracted data. We contacted study authors for further information with responses provided from three.

Main results

The review included nine studies; these studies differed in a variety of ways including definition of asthma exacerbations, FeNO cut-off levels used (12 parts per billion (ppb) to 30 ppb), the way in which FeNO was used to adjust therapy and duration of study (6 to 12 months). Of 1426 children randomised, 1329 completed the studies. The inclusion criteria for the participants in each study varied but all had a diagnosis of asthma. There was a significant difference in the number of children having one or more asthma exacerbations over the study period, they were significantly lower in the FeNO group in comparison to the control group (odds ratio (OR) 0.58, 95% confidence interval (CI) 0.45 to 0.75; 1279 participants; 8 studies). The number needed to treat for an additional beneficial outcome (NNTB) over 52 weeks was 9 (95% CI 6 to 15). There was no difference between the groups when comparing exacerbation rates (mean difference (MD) -0.37, 95% CI -0.8 to 0.06; 736 participants; 4 studies; $I^2 = 67%$). The number of children in the FeNO group requiring oral corticosteroid courses was lower in comparison to the children in the control group (OR 0.63, 95% CI 0.48 to 0.83; 1169 participants; 7 studies; $I^2 = 0%$). There was no statistically significant difference between the groups for exacerbations requiring hospitalisation (OR 0.75, 95% CI 0.41 to 1.36; 1110 participants; 6 studies; $I^2 = 0%$). There were no significant differences between the groups for any of the secondary outcomes (forced expiratory volume in one second (FEV_1), FeNO levels, symptom scores or inhaled corticosteroid doses at final visit). The included studies recorded no adverse events.

Three studies had inadequate blinding and were thus considered to have a high risk of bias. However, when these studies were removed in subgroup analysis, the difference between the groups for the primary outcome (exacerbations) remained statistically significant. The GRADE quality of the evidence ranged from moderate (for the outcome 'Number of participants who had one or more exacerbations over the study period') to very low (for the outcome 'Exacerbation rates'), based on lack of blinding, statistical heterogeneity and imprecision.

Authors' conclusions

In this updated review with five new included studies, tailoring asthma medications based on FeNO levels (in comparison with primarily guideline management) significantly decreased the number of children who had one or more exacerbations over the study period but did not impact on the day-to-day clinical symptoms or inhaled corticosteroid doses. Therefore, the use of FeNO to guide asthma therapy in children may be beneficial in a subset of children, it cannot be universally recommended for all children with asthma.

Further RCTs need to be conducted and these should encompass different asthma severities, different settings including primary care and less affluent settings, and consider different FeNO cut-offs.

Summary of Petsky et al. Meta-analysis



- Included 9 studies conducted among children
- 1,426 patients were randomized
- 1,329 completed the study
- Odds of reducing asthma exacerbations (# of patients with ≥ 1 exacerbation) using FeNO vs. symptoms-based approach
- Odds ratio (OR) = 0.58 (95% CI, 0.45-0.75)
- Number Needed to Benefit (NNTB) in one year = 9 (95% CI, 6-15)
- FeNO-aided management significantly reduced asthma exacerbations compared to a guidelines-only based approach

Exhaled nitric oxide reflects asthma severity and asthma control

Claudia Delgado-Corcoran, MD, MPH, FAAP; Niranjana Kissoon, MD, CPE, FAAP, FCCM, FRCPC;
Suzanne P. Murphy, PhD; Laurie J. Duckworth, RN, BSN, CCRC

Introduction: This study was undertaken to a) evaluate whether exhaled nitric oxide (fraction of exhaled nitric oxide [FENO]) levels are reflective of asthma severity in concordance with the National Asthma Education and Prevention Program categorization and b) determine the usefulness of FENO using the single-breath exhalation technique for monitoring asthma control and compliance with steroid treatment.

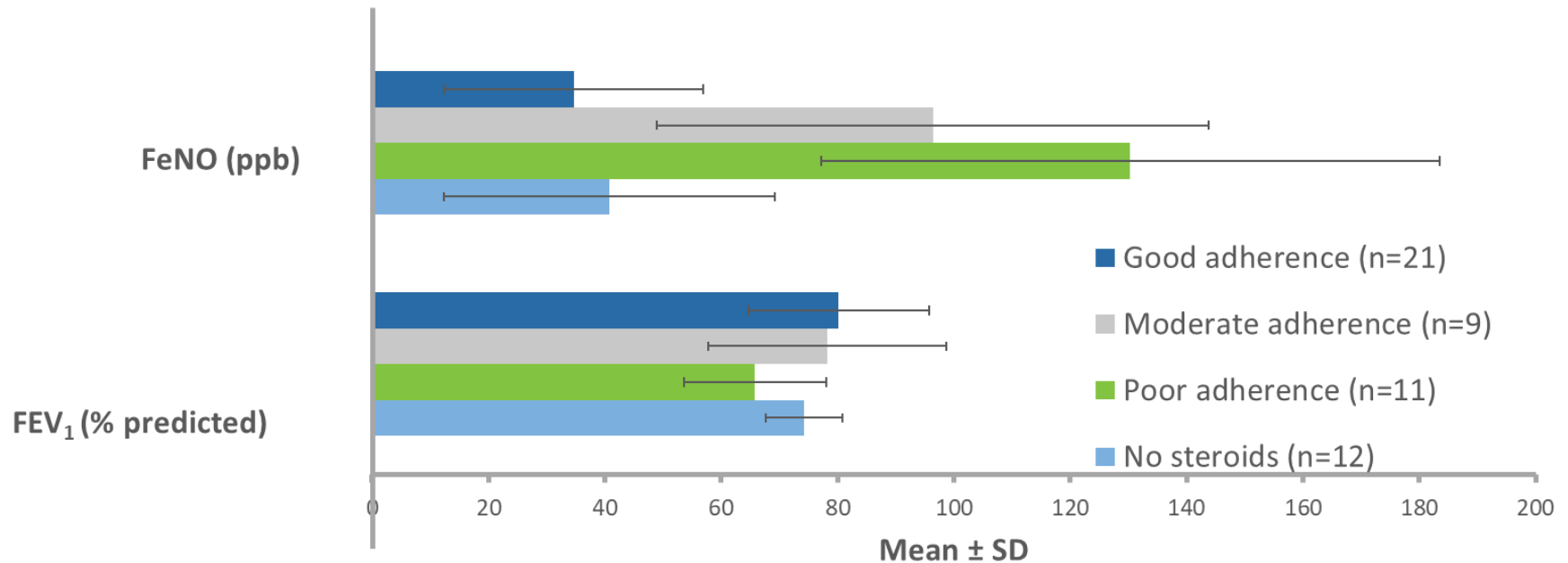
Methods: Thirty patients with asthma (7–17 yrs old; 14 males and 16 females) that was mild ($n = 8$), moderate ($n = 17$), or severe ($n = 5$) were included in the study. Fifteen patients were seen on more than one occasion for a total of 53 visits. Information obtained at each visit included asthma symptoms, β -agonists and corticosteroids use, compliance to steroids, and forced expiratory volume in 1 sec (FEV_1) and FENO measurements. Asthma control was judged by a pulmonologist based on overall evaluation of symptoms, FEV_1 measurements, and the frequency of β -agonists use at each visit.

Results: The mean \pm SD FENO was significantly different in the mild, moderate, and severe asthma categories (30 ± 12 , 65 ± 48 , 104 ± 68 , respectively; $F_{2,52} = 6.02$ $p = .005$). FENO was significantly correlated with asthma severity ($r = .44$, $p = .001$), compliance ($r = -.75$, $p = .001$), and control ($r = -.51$, $p = .001$). There were no statistically significant differences between asthma severity and compliance or FEV_1 .

Discussion: Our data suggest that a) FENO may be a practical tool to evaluate asthma severity and asthma control over time and b) FENO may be used as a marker of compliance with steroids even when FEV_1 has not decreased significantly. (Pediatr Crit Care Med 2004; 5:48–52)

KEY WORDS: exhaled nitric oxide; asthma; asthma severity; asthma categorization; inflammation

Examined Utility of FeNO for monitoring ICS treatment adherence in 30 children (aged 7-17 years) with asthma



- Mean FeNO levels were significantly reduced in patients with good ICS adherence^{*†}
- FEV₁ levels were not substantially different among adherence groups

FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; ppb, parts per billion.

^{*}Adherence determined by calculating number of doses per day and number prescribed. Good, moderate, and poor adherence defined as >75% adherence, 50% to 75% adherence, and <49% adherence to prescribed medication, respectively. [†]Compared with patients with poor ($P=0.001$) and moderate ($P=0.013$) adherence.

1. Delgado-Corcoran et al. *Pediatr Crit Care Med*. 2004;5:48-52.

Table 2. FENO and FEV₁ vs. compliance with steroid treatment (mean ± sd)

	Compliance Category			
	Poor (n = 11)	Moderate (n = 9)	Good (n = 21)	No Steroids (n = 12)
FEV ₁ , % predicted	65.82 ± 12.29	78.24 ± 20.47	80.19 ± 15.52	74.29 ± 6.56
FENO, ppb	130.30 ± 53.16 ^a	96.37 ± 47.39	34.65 ± 22.25 ^b	40.76 ± 28.38

^ap = .001 compared with poor and good; ^bp = .013 compared with moderate and good.

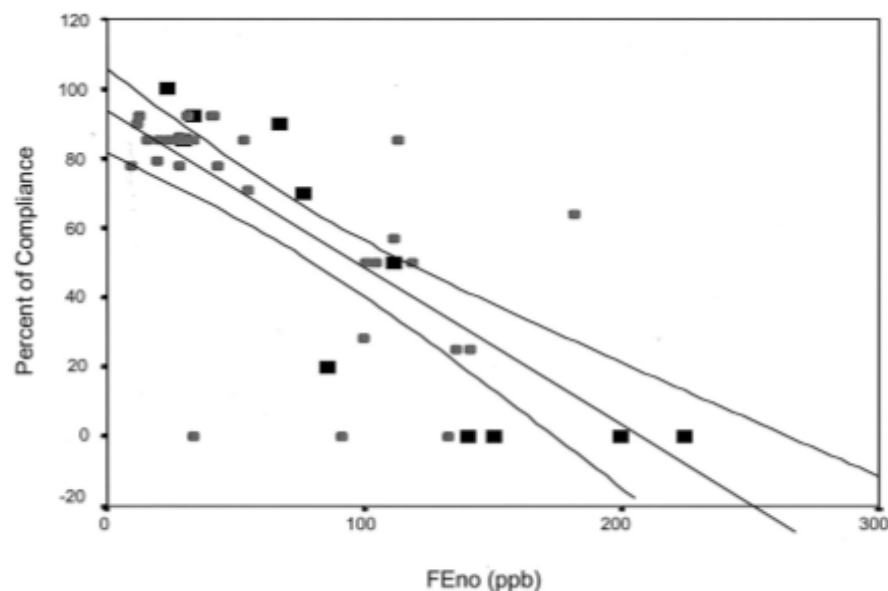


Figure 1. Relationship between fraction of exhaled nitric oxide (FENO) and compliance (n = 41 visits). Squares, severe asthma; circles, moderate asthma; ppb, parts per billion.

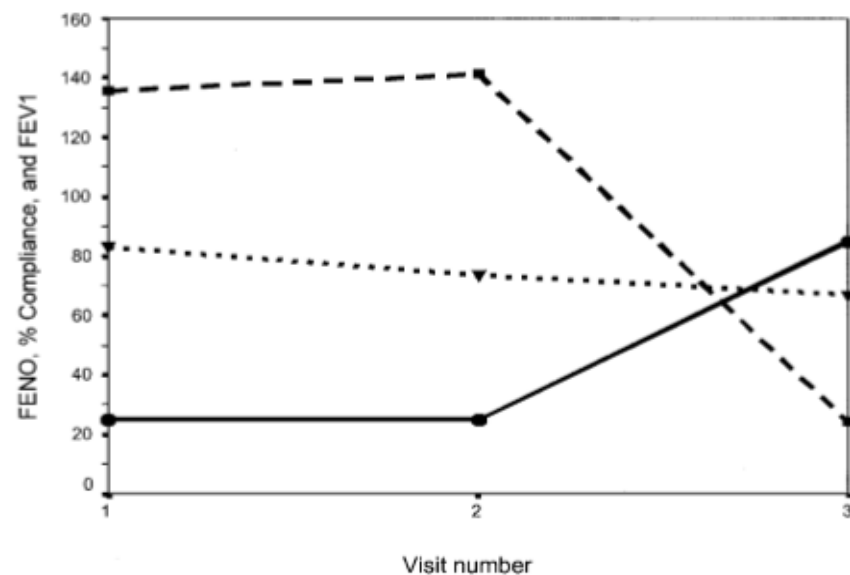
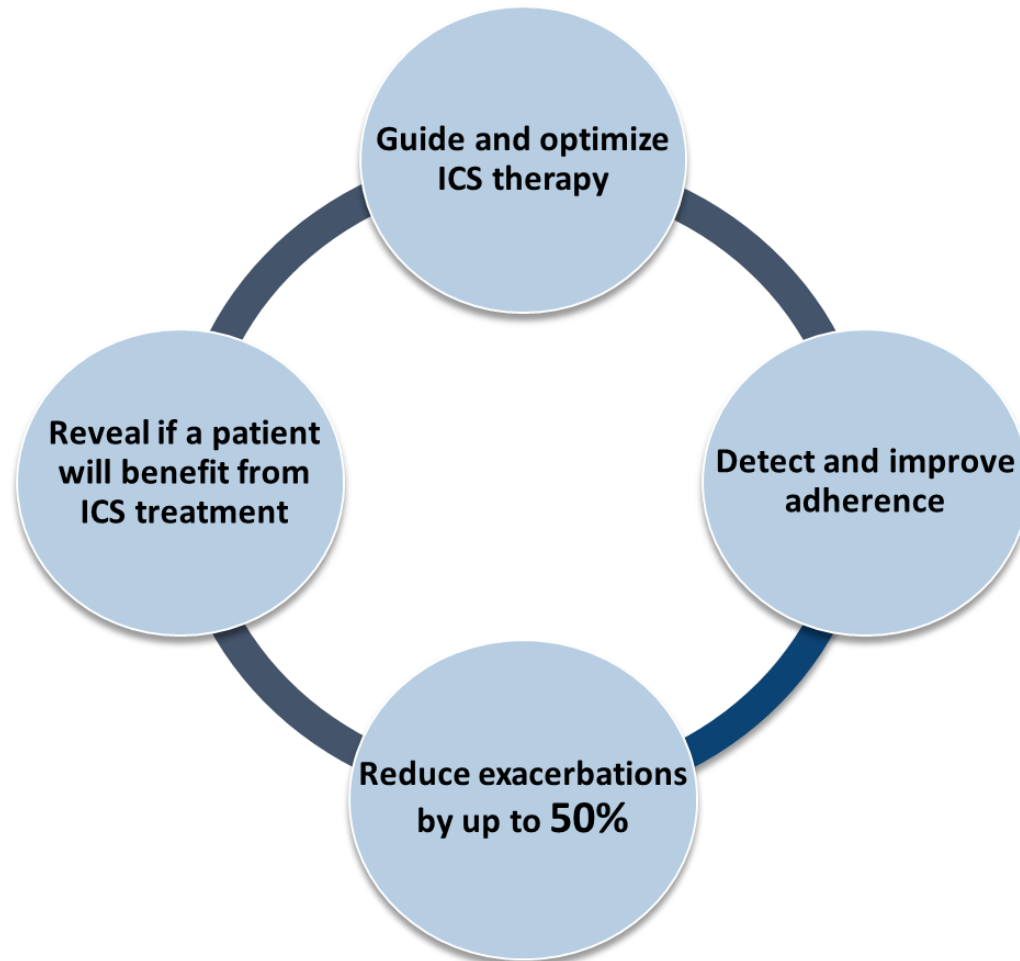
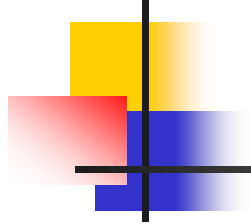


Figure 2. Relationship between fraction of exhaled nitric oxide (FENO), forced expiratory volume in 1 sec (FEV₁), and compliance for one patient during three visits. Squares, FENO; triangles, FEV₁; circles, percentage compliance.

Benefits of Routine FeNO Monitoring





Remote Electronic Sensors



Rationale for Remote Electronic Sensors

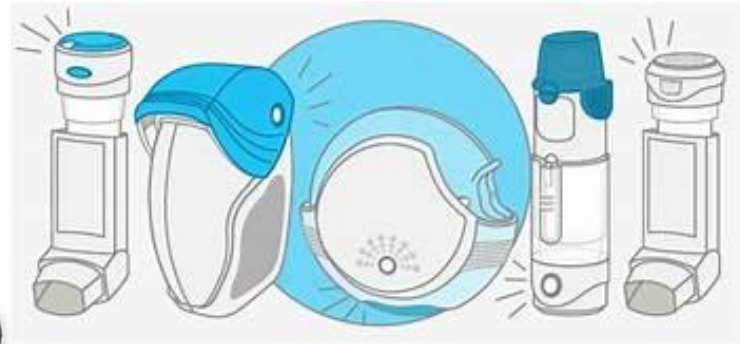
- Adherence to ICS therapy is frequently low ($\leq 50\%$)
- Suboptimal adherence undermines therapy effectiveness, results in greater morbidity & more frequent HC visits
- Asthma management guidelines recommend that clinicians monitor & stimulate ICS medication adherence
- Clinicians do not detect ICS non-adherence at rates that exceed those predicted by chance alone
- Parent/school reports, treatment diaries, questionnaires, canister weight, and pill counts all over-estimate adherence
- Most methods fail to detect 'dumping', 'white coat effect', 'drug holidays'
- Remote electronic monitoring the most objective and empirical way to measure ICS adherence
- Being informant-free & non-intrusive, remote e-sensors capture "real time" adherence, regardless of who administers the medication

Typical Components of E-monitoring System



- ❑ Bluetooth-enabled 'smart' e-sensor attached to all the inhalers (rescue & maintenance)
- ❑ Smartphone-based mobile application synced with e-sensor and remote cloud-based server
- ❑ ± Miniature digital spirometer/spacer
- ❑ ± Digital hygrometer or 'air quality' monitor
- ❑ Unique 'dashboards' for child/parent, pediatrician, case manager, school nurse, asthma educator, respiratory therapist, home 'visitor'

Propeller Health Smart Sensors





How Propeller Sensor Works

<https://youtu.be/iq7bWPPRDzs>

Feasibility of Deploying Inhaler Sensors to Identify the Impacts of Environmental Triggers and Built Environment Factors on Asthma Short-Acting Bronchodilator Use

Jason G. Su,¹ Meredith A. Barrett,² Kelly Henderson,² Olivier Humblet,² Ted Smith,³ James W. Sublett,⁴ LaQuandra Nesbitt,⁵ Chris Hogg,² David Van Sickle,^{2,6} and James L. Sublett⁴

BACKGROUND: Epidemiological asthma research has relied upon self-reported symptoms or healthcare utilization data, and used the residential address as the primary location for exposure. These data sources can be temporally limited, spatially aggregated, subjective, and burdensome for the patient to collect.

OBJECTIVES: First, we aimed to test the feasibility of collecting rescue inhaler use data in space–time using electronic sensors. Second, we aimed to evaluate whether these data have the potential to identify environmental triggers and built environment factors associated with rescue inhaler use and to determine whether these findings would be consistent with the existing literature.

METHODS: We utilized zero-truncated negative binomial models to identify triggers associated with inhaler use, and implemented three sensitivity analyses to validate our findings.

RESULTS: Electronic sensors fitted on metered dose inhalers tracked 5,660 rescue inhaler use events in space and time for 140 participants from 13 June 2012 to 28 February 2014. We found that the inhaler sensors were feasible in passively collecting objective rescue inhaler use data. We identified several environmental triggers with a positive and significant association with inhaler use, including: AQI, PM₁₀, weed pollen, and mold. Conversely, the spatial distribution of tree cover demonstrated a negative and significant association with inhaler use.

CONCLUSIONS: Utilizing a sensor to capture the signal of rescue inhaler use in space–time offered a passive and objective signal of asthma activity. This approach enabled detailed analyses to identify environmental triggers and built environment factors that are associated with asthma symptoms beyond the residential address. The application of these new technologies has the potential to improve our surveillance and understanding of asthma.

CITATION: Su JG, Barrett MA, Henderson K, Humblet O, Smith T, Sublett JW, Nesbitt L, Hogg C, Van Sickle D, Sublett JL. 2017. Feasibility of deploying inhaler sensors to identify the impacts of environmental triggers and built environment factors on asthma short-acting bronchodilator use. *Environ Health Perspect* 125:254–261; <http://dx.doi.org/10.1289/EHP266>



Effect of a mobile health, sensor-driven asthma management platform on asthma control

Meredith A. Barrett, PhD^{*}; Olivier Humblet, ScD^{*}; Justine E. Marcus, BA[†]; Kelly Henderson, MPH^{*}; Ted Smith, PhD[‡]; Nembr Eid, MD[§]; J. Wesley Sublett, MD, MPH^{||}; Andrew Renda, MD, MPH[¶]; LaQuandra Nesbitt, MD, MPH^{#,***}; David Van Sickle, PhD^{††,‡‡}; David Stempel, MD^{*}; James L. Sublett, MD^{||}

A B S T R A C T

Background: Asthma inflicts a significant health and economic burden in the United States. Self-management approaches to monitoring and treatment can be burdensome for patients.

Objective: To assess the effect of a digital health management program on asthma outcomes.

Methods: Residents of Louisville, Kentucky, with asthma were enrolled in a single-arm pilot study. Participants received electronic inhaler sensors that tracked the time, frequency, and location of short-acting β -agonist (SABA) use. After a 30-day baseline period during which reference medication use was recorded by the sensors, participants received access to a digital health intervention designed to enhance self-management. Changes in outcomes, including mean daily SABA use, symptom-free days, and asthma control status, were compared among the initial 30-day baseline period and all subsequent months of the intervention using mixed-model logistic regressions and χ^2 tests.

Results: The mean number of SABA events per participant per day was 0.44 during the control period and 0.27 after the first month of the intervention, a 39% reduction. The percentage of symptom-free days was 77% during the baseline period and 86% after the first month, a 12% improvement. Improvement was observed throughout the study; each intervention month demonstrated significantly lower SABA use and higher symptom-free days than the baseline month ($P < .001$). Sixty-nine percent had well-controlled asthma during the baseline period, 67% during the first month of the intervention. Each intervention month demonstrated significantly higher percentages than the baseline month ($P < .001$), except for month 1 ($P = .80$).

Conclusion: A digital health asthma management intervention demonstrated significant reductions in SABA use, increased number of symptom-free days, and improvements in asthma control.

Trial Registration: [ClinicalTrials.gov](https://clinicaltrials.gov) Identifier: NCT02162576.

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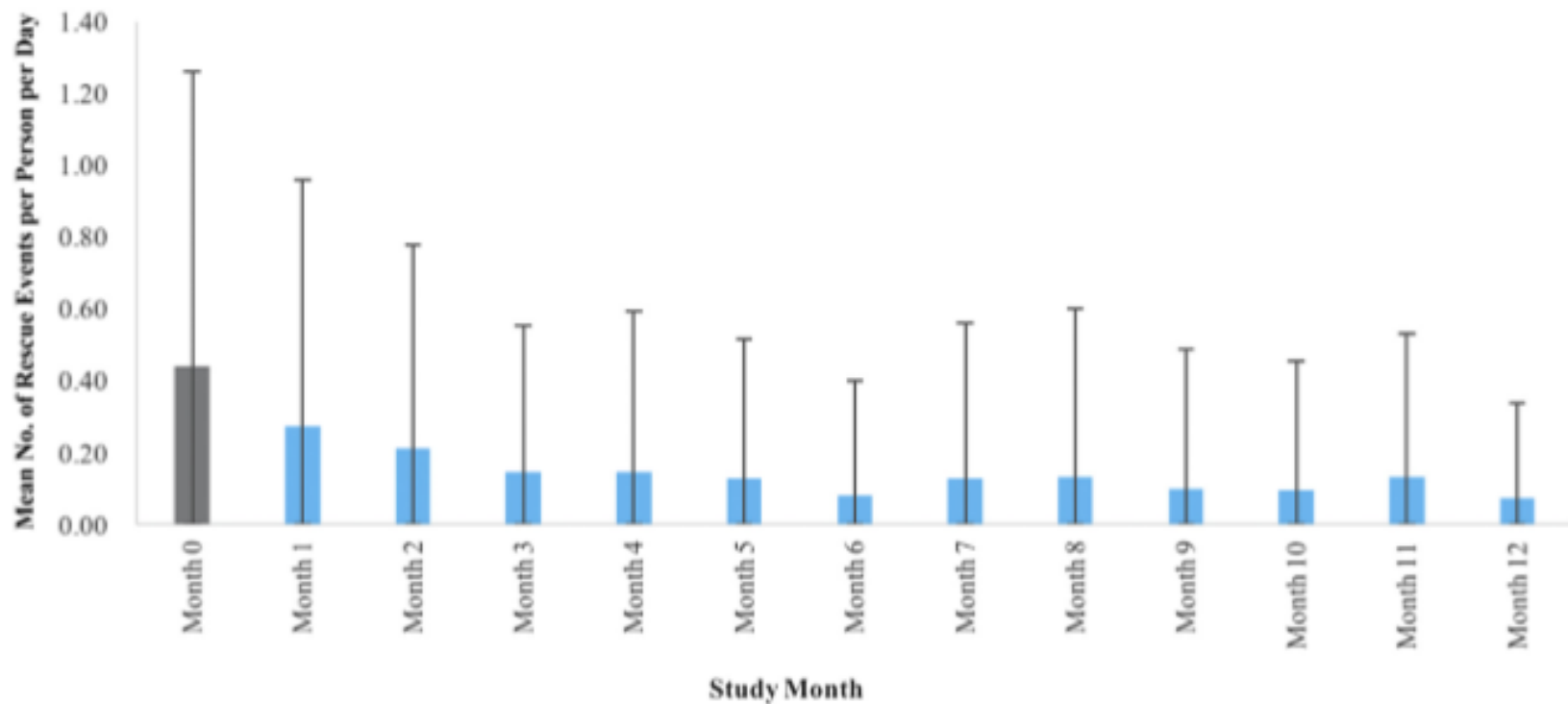


Figure 2. Mean short-acting β -agonist use per active participant per day of the program, aggregated by month, with error bars representing 1 SD.

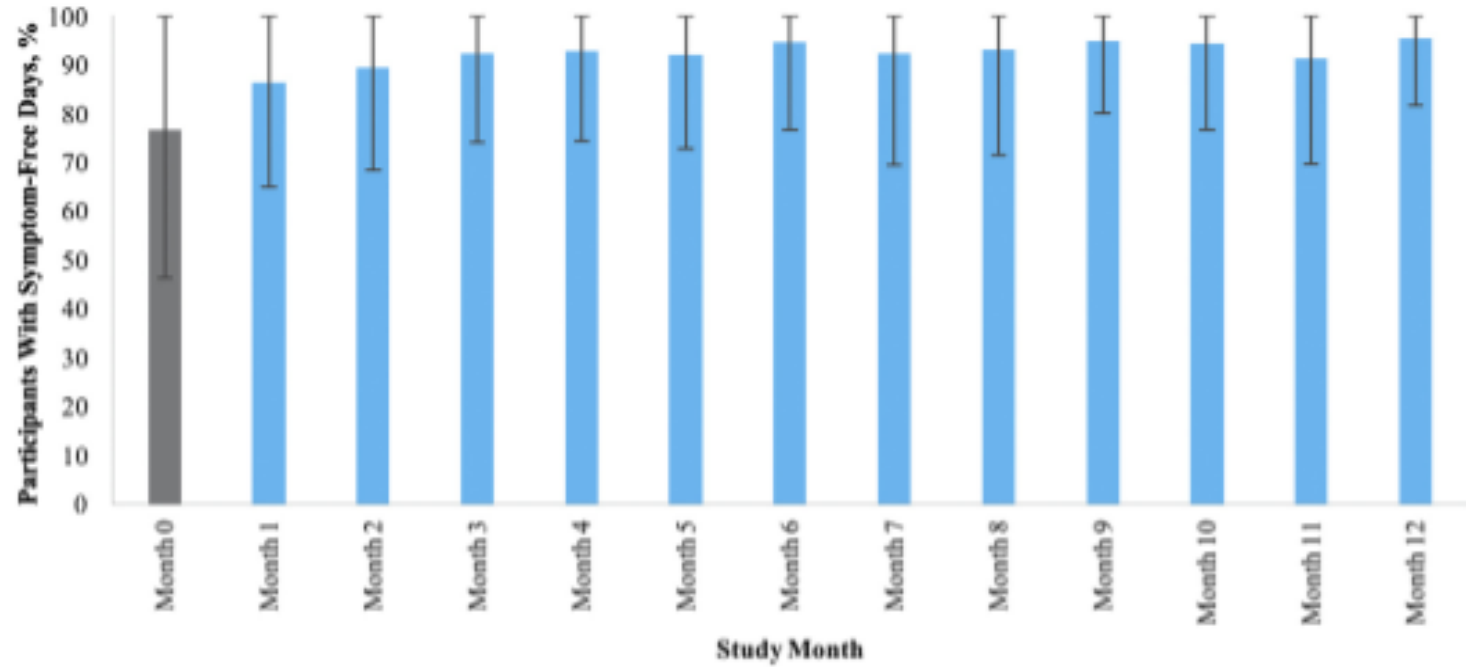


Figure 3. Percentage of active participants with a symptom-free day for each day of the program, aggregated by study month, with error bars representing 1 SD.

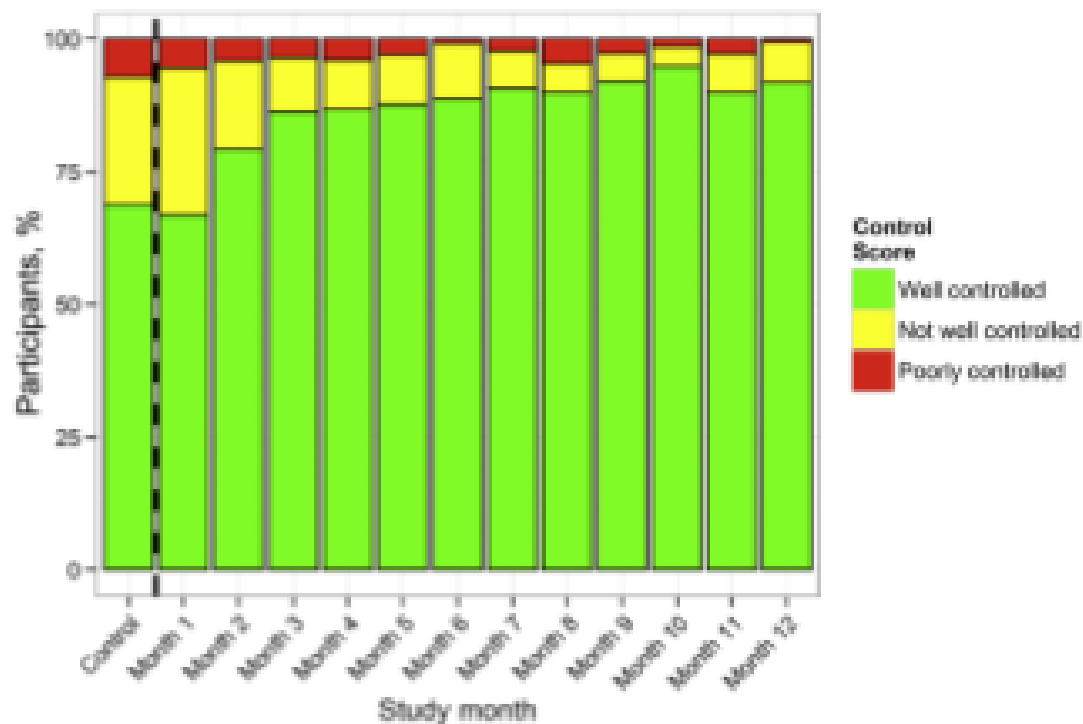


Figure 4. Percentage of participants with well-controlled, not well-controlled, and poorly controlled asthma, aggregated by study month.



Impact of a digital health intervention on asthma resource utilization

Rajan Merchant¹, Stanley J. Szefler², Bruce G. Bender³, Michael Tuffli⁴, Meredith A. Barrett⁴, Rahul Gondalia^{4*},
Leanne Kaye⁴, David Van Sickle⁵ and David A. Stempel⁴

Abstract

Digital health interventions have been associated with reduced rescue inhaler use and improved controller medication adherence. This quality improvement project assessed the benefit of these interventions on asthma-related healthcare utilizations, including hospitalizations, emergency department (ED) utilization and outpatient visits. The intervention consisted of electronic medication monitors (EMMs) that tracked rescue and controller inhaler medication use, and a digital health platform that presented medication use information and asthma control status to patients and providers. In 224 study patients, the number of asthma-related ED visits and combined ED and hospitalization events 365 days pre- to 365 days post-enrollment to the intervention significantly decreased from 11.6 to 5.4 visits ($p < 0.05$) and 13.4 to 5.8 events ($p < 0.05$) per 100 patient-years, respectively. This digital health intervention was successfully incorporated into routine clinical practice and was associated with lower rates of asthma-related hospitalizations and ED visits.

Keywords: Telemedicine, Delivery of health care, Pulmonary medicine, Asthma, Digital health

Table 2 Pre- versus post-enrollment year rates (95% confidence intervals) in asthma-related utilization

	Pre-enrollment	Post-enrollment	Rate Difference
Hospitalizations	1.8 (0.5, 4.6)	0.4 (0.01, 2.5)	1.3 (-0.6, 3.3)
Emergency department (ED) visits	11.6 (1.6, 17.0)	5.4 (2.8, 9.4)	6.3 (0.9, 11.6)
ED + Hospitalizations	13.4 (9.0, 19.1)	5.8 (3.1, 9.2)	7.6 (1.9, 13.3)

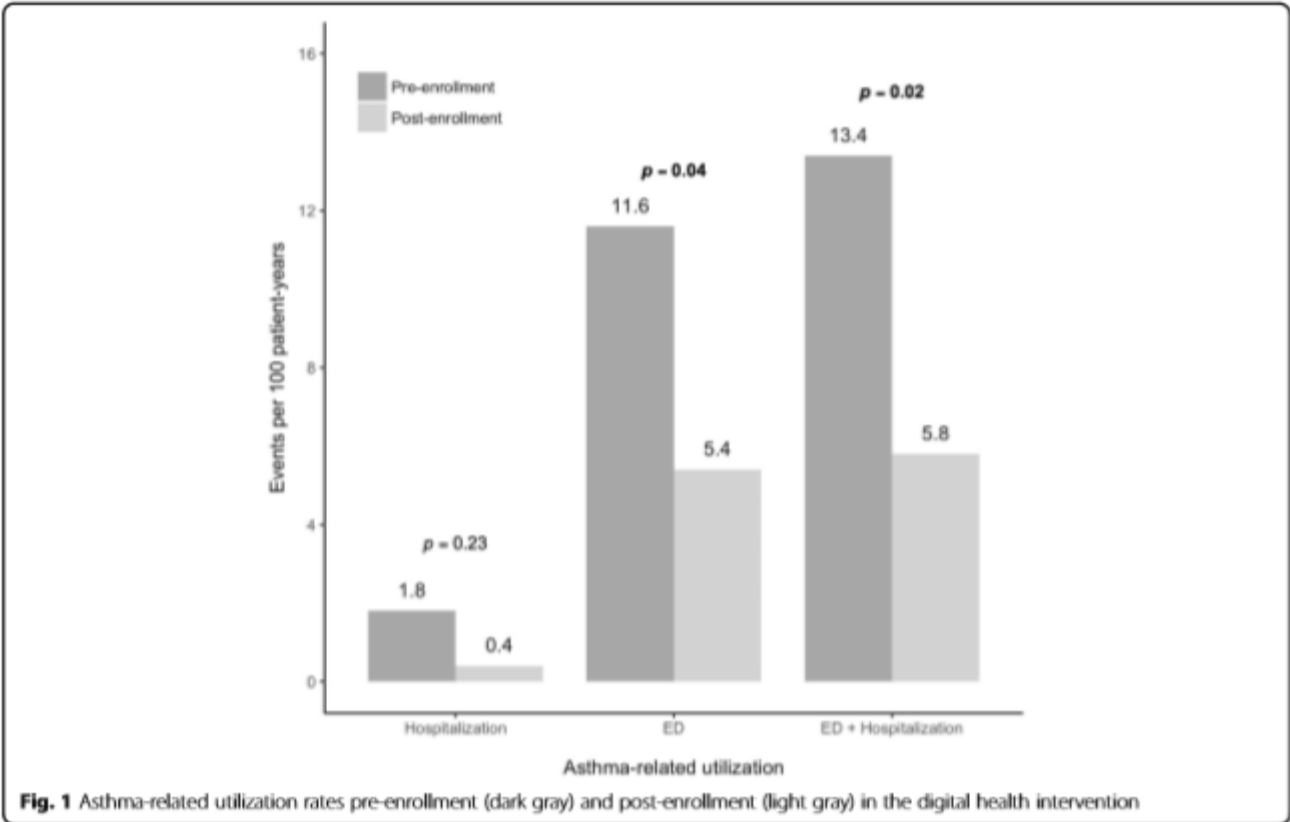


Fig. 1 Asthma-related utilization rates pre-enrollment (dark gray) and post-enrollment (light gray) in the digital health intervention

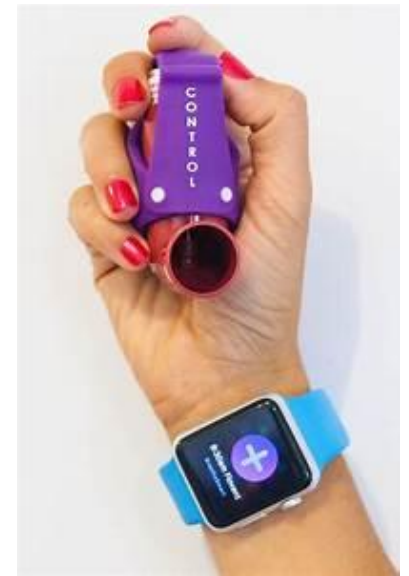


Table 3 Inhaler use improvements from week 1 to 52 following enrollment in the digital health intervention

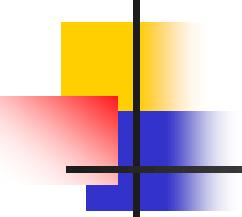
	Week 1	Week 52	Difference	Percent change
SABA puffs/day	0.68	0.16	0.52 (95% CI: 0.34, 0.69)*	+ 76%
Controller-to-total medication ratio	0.66	0.82	-0.16 (95% CI: -0.25, -0.07)*	- 24%

* $p < 0.01$

Cohero Health Asthma Care Platform



Feasibility of a novel mHealth management system to capture and improve medication adherence among adolescents with asthma



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Andrew Ting³
Michael K Parides¹

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Purpose: Currently, 7.1 million children in the United States have asthma. Nonadherence to daily controller asthma medication is common, leading to more severe symptoms, overuse of rescue medication, and increased hospitalizations. The purpose of this study was to develop and evaluate the feasibility and acceptability of a novel mHealth management system composed of a sensed device, which is connected to mobile phone app that is designed to monitor and improve asthma medication adherence.

Patients and methods: The asthma management system was designed using well-established behavioral theory. Seven adolescents aged 11–18 years were enrolled and given an adherence sensor, and four of those also received a mobile phone app with game features and reminders. Five patients completed the study, and one was lost to follow-up in each group. Mobile app users and their parents participated in focus groups to assess patient preferences. Feasibility was assessed by the ability of sensors to capture real-time medication data. Acceptability was assessed by patient questionnaire and focus group analysis.

Results: Successful upload of real-time data from six of seven inhaler sensors to the HIPAA-compliant server demonstrates the feasibility of at-home patient monitoring using the sensor device. All three mobile app users who completed the study reported interest in continued use of the management system and would recommend the app to friends. Unstructured interviews and focus groups revealed that patients felt that the intervention helped their sense of asthma control.

Conclusion: This study demonstrates the feasibility of using the sensor device to remotely monitor real-time medication usage, and user feedback demonstrates the acceptability of the intervention for patient use. The findings provide guidance for the improvement of study design and technology development. Further research is needed to assess the efficacy of the intervention.

Keywords: asthma control, medication adherence, patient engagement, patient monitoring, mobile health



Understanding clinicians' attitudes toward a mobile health strategy to childhood asthma management: A qualitative study

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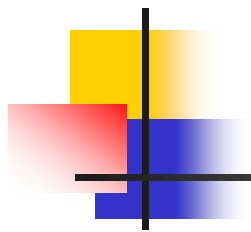
ABSTRACT

Objectives: Mobile technology for childhood asthma can provide real-time data to enhance care. What real-time adherence information clinicians want, how they may use it, and if the data meet their clinical needs have not been fully explored. Our goal was to determine whether pediatric primary care and pulmonary clinicians believe if a sensor-based mobile intervention is useful in caring for patients with asthma. **Methods:** We recruited participants from 3 urban, primary care and 1 pulmonary practice from July to September 2015 in Hartford, CT. Forty-one participated in four focus groups, which included a demonstration of the technology. Participants were probed with open-ended questions on the type, frequency, and format of inter-visit patient information they found useful. **Results:** 41 participants (mean age 49 (\pm 13.7) years) were board-certified clinicians (41% MDs and 20% mid-level practitioners), practiced medicine on an average of 19 (\pm 14) years, were primarily white (59%) and women (78%). Clinicians wanted 1) adherence to prescribed inhaler therapy and 2) data on inhaler technique. Clinicians wanted it at the time of a scheduled clinic visit but also wanted inter-visit alerts for excessive use of rescue therapy. Pulmonologists liked the mobile spirometer's provision of inter-visit lung function data; pediatricians did not share this view. Concerns with data accuracy were raised due to families who shared inhalers, access to smartphones, and protection of health information. **Conclusions:** Overall, clinicians view an asthma mobile health technology as enhancing the patient-centered medical home. Pediatric primary care clinicians and pulmonologists want different information from a mobile app.

Key Findings from Hollenbach *et al.* Focus Group Study



- Key benefit of mHealth platform is real-time adherence data that can be pushed directly into the HER
- Data can be viewed either during a scheduled clinic visit or after a customizable, patient-specific threshold is met
- Ability of app to collect, store, and display long-term data of seasonal, patient, and practice trends is an educational tool that could inform quality improvement efforts
- Concerns about data accuracy due to families presumed inhaler-sharing practices
- Concerns about protecting patient privacy
- mHealth app seen as adding value to clinician's provision of high-quality asthma care



Thank You!