Evidence-Based Asthma Management

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In 2002 the National Asthma Education and Prevention Program published evidence-based guidelines for the diagnosis and management of asthma, but there are some unresolved asthma-management issues that need further research. For asthmatic children inhaled corticosteroids are more beneficial than as-needed use of β_2 agonists, long-acting β_2 agonists, theophylline, cromolyn sodium, nedocromil, or any combination of those. Leukotriene modifiers are an alternative but not a preferred treatment; they should be considered if the medication needs to be administered orally rather than via inhalation. Cromolyn sodium and nedocromil are effective long-term asthma-control medications, but they are not as effective as inhaled corticosteroids. There is insufficient evidence to determine whether cromolyn benefits maintenance of childhood asthma. Cromolyn sodium and nedocromil are alternatives, but not preferred treatments for mild persistent asthma. Cromolyn may be useful as a preventive therapy prior to exertion or unavoidable exposure to allergens. Regular inhalation of corticosteroids controls asthma significantly better than as-needed β_2 agonists. No studies have examined the long-term impact of regular inhaled corticosteroids on lung function in children $\leq$ 5 years old. As monotherapy, inhaled corticosteroids are more effective than long-acting β_2 agonists. The asthma-control benefit of inhaled corticosteroids decidedly outweighs the risks from inhaled corticosteroids. There is no high-level evidence that low-to-medium-dose inhaled corticosteroids have ocular toxicity or important effects on hypothalamic-pituitary-adrenal function in children. Antibiotic therapy has no role in asthma management unless there is a bacterial comorbidity, but further research is needed on the relationship between sinusitis and asthma exacerbation. The asthma care plan should include a written asthma action plan for the patient, but there is inadequate evidence as to whether the asthma action plan should be based on symptoms or on peak flow monitoring. There is low-level evidence that helium-oxygen mixture (heliox) may be of benefit in the first hour of an acute asthma attack but less advantageous after that first hour. Metered-dose inhalers are no more or less effective, overall, than other aerosol-delivery devices for the delivery of β_2 agonists or inhaled corticosteroids, so the least expensive delivery method should be chosen. *Key words: asthma, corticosteroid, β agonist, antibiotic, metered-dose inhaler, heliox, evidence-based medicine.* [Respir Care 2004;49(7):783–792.

Introduction

The evidence-based-medicine approach is that treatments and disease-management strategies should be supported by evidence from rigorous, reproducible, peer-reviewed research. A clinician's personal observations of a treatment's apparent efficacy in some (or even many) patients is not adequate evidence, partly because clinicians rarely get to observe the important medium-term and long-term outcomes that really matter to the patient, such as sustained relief of symptoms and quality of life, but instead tend to focus on physiologic measurements such as blood oxygen saturation. Evidence-based medicine requires ranking the evidence. The best evidence is from large, randomized controlled trials, whereas the least trusted evidence is expert opinion. The evidence-based-medicine approach often disabuses us of unfounded beliefs and assumptions about treatments and disease management strategies; our preconceived notions often do not stand up against high-level evidence. This report reviews the evidence regarding asthma management.

The prevalence of asthma has grown markedly and there has been increased emphasis on early identification and treatment. In the United States approximately 15 million people have asthma. Asthma annually causes about 5,400 deaths, about 500,000 hospitalizations, and about 2 million emergency department visits. It affects all age groups, but its prevalence is particularly increasing in the pediatric population: about 5% of children have it.

Role of the NHLBI and the NAEPP

In the late 1980s the National Heart, Lung, and Blood Institute (NHLBI) recognized the asthma trends and convened the National Asthma Education and Prevention Program (NAEPP), with the goal of educating the public and professionals about asthma. The NAEPP includes 35 member organizations, with representatives from government, academic, and other health-related institutions, such as the American Association for Respiratory Care.

In 1991 the NAEPP published a landmark document, the NAEPP Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma,[1–3] which was revised and published again in 1997 and 2002. The NAEPP Expert Panel Report was approved by the NAEPP Coordinating Committee, which convened a scientific committee from its membership, with representatives from all aspects of asthma management. The committee initially reviewed over 5,000 asthma-related documents, of which 688 were selected for more in-depth review; from those 688 reports, 87 were selected for systematic review. The present review relies largely on the 2002 version of the NAEPP Expert Panel Report and describes current evidence-based treatment and management strategies for asthma. I will address inhaled corticosteroids, β agonists, antibiotics, asthma action plans, helium-oxygen mixture (heliox), and aerosol delivery devices.

Inhaled Corticosteroids

The 1991 and 1997 NAEPP Expert Panel Reports recommended inhaled corticosteroids for asthma, but that recommendation was not supported by high-level evidence until the 2002 revision of the Expert Panel Report. Of particular interest to the panel was the role of inhaled corticosteroids in long-term outcomes of children who suffer mild-to-moderate persistent asthma. The primary question was, among those children does long-term, regular use of inhaled corticosteroids provide more benefit than as-needed use of β_2 agonists, long-acting β_2 agonists, theophylline, cromolyn sodium, nedocromil, or some combination of those? In their literature review the panel found strong evidence that inhaled corticosteroids improve long-term outcomes for asthmatic children. High-level evidence (ie, from randomized controlled trials) indicates that inhaled corticosteroids are associated with fewer hospitalizations, fewer urgent care visits, better symptom scores, fewer oral steroid bursts, and better forced expiratory volume in the first second (FEV_1) before and after treatment, and none of the other asthma medications were as effective as inhaled corticosteroids in improving the asthma outcomes of interest. Leukotriene modifiers were not included in that review because none of the published data on leukotriene modifiers met the review inclusion criteria. The panel opined that leukotriene modifiers should be considered an alternative but not a preferred treatment, and they should be considered if the medication needs to be administered orally rather than via inhalation.

Cromolyn sodium and nedocromil are effective long-term asthma-control medications, but they are not as effective as inhaled corticosteroids.[4] A review by Tasche et al[5] concluded that there is insufficient evidence to determine whether cromolyn benefits the maintenance of childhood asthma. As with leukotriene modifiers, the panel recommended cromolyn sodium and nedocromil as alternatives but not as preferred drugs for mild persistent asthma and that cromolyn sodium may be useful as a preventive therapy prior to exertion or unavoidable exposure to allergens (this is an important change in the panel's long-term asthma-management guidelines). The panel's 2002 revised guidelines state that inhaled cor-

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Table 1. Stepwise Approach for Managing Acute or Chronic Asthma in Infants and Children 5 Years and Younger

Classify Severity: Clinical Features Before Treatment or Adequate Control			Medications Required to Maintain Long-Term Control
	Symptoms		Daily Medications
	Day	Night	
Severe Persistent	Continual	Frequent	Preferred treatment: High-dose inhaled corticosteroids AND Long-acting inhaled β_2 agonists AND, if needed, Corticosteroid tablets or syrup long-term (2 mg/kg/d, generally not to exceed 60 mg/d). Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.
Moderate Persistent	Daily	> 1 night/wk	Preferred treatment: Low-dose inhaled corticosteroids and long-acting inhaled β_2 agonists OR Medium-dose inhaled corticosteroids Alternative treatment: Low-dose inhaled corticosteroids and either leukotriene-receptor antagonist or theophylline. If needed (particularly in patients with recurring severe exacerbations): Preferred treatment: Medium-dose inhaled corticosteroids and long-acting β_2 agonists. Alternative treatment: Medium-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline
Mild Persistent	> 2/wk but < 1/d	> 2 nights/mo	Preferred treatment: Low-dose inhaled corticosteroids (with nebulizer or MDI with holding chamber, with or without face mask or DPI) Alternative treatment: Cromolyn (nebulizer is preferred or MDI with holding chamber) OR leukotriene receptor antagonist
Mild Intermittent	≤ 2 d/wk	≤ 2 nights/mo	No daily medications needed
All Patients	Bronchodilator as needed for symptoms. Intensity of treatment depends on severity of exacerbation. Preferred treatment: Short-acting inhaled β_2 agonists via nebulizer or face mask and holding chamber Alternative treatment: Oral β_2 agonists With viral respiratory infection: Bronchodilator every 4–6 h up to 24 h (longer with physician consult); in general, repeat no more than once every 6 weeks. Consider systemic corticosteroid if exacerbation is severe or patient has history of previous severe exacerbations. Use of short-acting β_2 agonists >2/wk for intermittent asthma (daily or increasing use in persistent asthma) may indicate the need to initiate (or increase) long-term-control therapy.		

MDI = metered-dose inhaler
DPI = dry powder inhaler
(Adapted from Reference 3.)

ticosteroids should be considered the first-line strategy for mild, moderate, and severe persistent asthma (inhaled corticosteroids had been considered second-line drugs).

Inhaled corticosteroids provide significantly better asthma control than as-needed β_2 agonists. No studies have examined the long-term impact of regular inhaled corticosteroids on lung function in children ≤ 5 years old.

Table 2. Stepwise Approach for Managing Acute or Chronic Asthma in Adults and Children Older Than 5 Years

Classify Severity: Clinical Features Before Treatment or Adequate Control					Medications Required To Maintain Long-Term Control
	Symptoms		PEF or FEV_1 (% of predicted)	PEF Variability (%)	Daily Medications
	Day	Night			
Severe Persistent	Continual	Frequent	≤ 60	> 30	Preferred treatment: High-dose inhaled corticosteroids AND Long-acting inhaled β_2 agonists AND, if needed, Corticosteroid tablets or syrup long-term (2 mg/kg/d, generally not to exceed 60 mg/d). Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.
Moderate Persistent	Daily	> 1 night/wk	> 60–< 80	> 30	Preferred treatment: Low-to-medium-dose inhaled corticosteroids and long-acting inhaled β_2 agonists. Alternative treatment: Increase inhaled corticosteroids within medium-dose range OR Low-medium dose inhaled corticosteroids and either leukotriene modifier or theophylline. If needed (particularly for patients who have recurring severe exacerbations): Preferred treatment: Increase inhaled corticosteroids within medium-dose range and add long-acting inhaled β_2 agonists. Alternative treatment: Increase inhaled corticosteroids within medium-dose range and add either leukotriene modifier or theophylline.
Mild Persistent	> 2/wk but < 1/d	> 2 nights/mo	≥ 80	20–30	Preferred treatment: Low-dose inhaled corticosteroids. Alternative treatment (listed alphabetically): Cromolyn, leukotriene modifier, nedocromil, OR Sustained-release theophylline to serum concentration of 5–15 μg/mL
Mild Intermittent	≤ 2 d/wk	≤ 2 nights/mo	≥ 80	< 20	No daily medications needed Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroids is recommended.
All Patients	Short-acting bronchodilator: 2–4 puffs short-acting β_2 agonist as needed for symptoms. Intensity of treatment depends on severity of exacerbation; up to 3 treatments at 20-min intervals or a single nebulizer treatment as needed. Course of systemic corticosteroids may be needed. Use of short-acting β_2 agonists more than twice a week for intermittent asthma (daily or increasing use in persistent asthma) may indicate the need to initiate (or increase) long-term-control therapy.				

PEF = peak expiratory flow
FEV_1 = forced expiratory volume in the first second.
(Adapted from Reference 3).

Inhaled Corticosteroids Versus Long-Acting β Agonists

As monotherapy, inhaled corticosteroids are more effective than long-acting β_2 agonists.[6] In a 16-week asthma-management study Lazarus et al found that clinical outcomes did not differ significantly between inhaled corticosteroids and long-acting β_2 agonists, but long-acting β_2 agonists were more likely to be associated with treatment failure and asthma exacerbation.

Table 3. Usual Dosages for Long-Term Asthma Control Medications*

Medication	Dose Form	Adult Dose	Child Dose†	Comments
Systemic Corticosteroids		Applies to All 3 Corticosteroids		
Methylprednisolone	Oral: 2, 4, 8, 16, 32 mg tablets	7.5–60 mg daily in a single dose in morning or 4 times/d, as needed for control.	0.25–2 mg/kg/d in A single dose in morning or 4 times/d, as needed for control.	For long-term treatment of severe persistent asthma, administer single dose in the morning, either daily or on alternate days (alternate-day therapy may cause less adrenal suppression). If daily doses are required, one study suggested better efficacy and no increase in adrenal suppression when administered at 3:00 pm. Short courses or "bursts" are effective for establishing control when initiating therapy or during a period of gradual deterioration.
Prednisolone	Oral: 5 mg tablets. 5 mg/5 mL, 15 mg/5 mL	Short-course "burst" to achieve control: 40–60 mg/d as single or 2 divided doses for 3–10 d.	Short-course "burst:" 1–2 mg/kg/d. Maximum: 60 mg/d for 3–10 d	
Prednisone	Oral: 1, 2.5, 5, 10, 20, 50 mg tablets, 5 mg/mL, 5 mg/5 mL			
Long-Acting Inhaled β_2 Agonists				Should not be used for symptom relief or exacerbations. Use with corticosteroids.
Salmeterol	DPI 50 μg/blister	1 blister every 12 h	1 blister every 12 h	May use 1 dose nightly for symptoms. Efficacy and safety have not been studied in children < 5 y old. Each capsule is for single use only; additional doses should not be administered for at least 12 h. Capsules should be used only with the Aerolizor inhaler and should not be taken orally.
Formoterol	DPI 12 μg per single-use capsule	1 capsule every 12 h	1 capsule every 12 h	
Combined Medications				
Fluticasone plus salmeterol	DPI 100 μg, 250 μg, or 500 μg/ 50 μg	1 inhalation twice a day. Dose depends on severity of asthma	1 inhalation twice a day. Dose depends on severity of asthma	Not approved by the Food and Drug Administration for children < 12 y old. 100/50 μg for patients not controlled on low-to-medium dose inhaled corticosteroids. 250/50 μg for patients not controlled on medium-to-high dose inhaled corticosteroids.
Cromolyn and Nedocromil				
Cromolyn	MDI 1 mg/puff Nebulizer: 20 mg/ ampule	2–4 puffs 3 or 4 times/d 1 ampule 3 or 4 times/d	1–2 puffs 3 or 4 times/d 1 ampule 3 or 4 times/d	One dose of either cromolyn or nedocromil prior to exercise or allergen exposure provides effective prophylaxis for 1–2 h.
Nedocromil	MDI 1.75 mg/puff	2–4 puffs 2 to 4 times/d	1–2 puffs 2 to 4 times/d	
Leukotriene Modifiers				
Montelukast	4 mg or 5 mg chewable tablet, 10 mg tablet	10 mg at bedtime	4 mg at bedtime (2–5 y old) 5 mg at bedtime (6–14 y old) 10 mg at bedtime (> 14 y old)	Montelukast exhibits a flat dose-response curve. Doses > 10 mg will not produce a greater response in adults.
Zafirlukast	10 or 20 mg tablet	40 mg daily (20 mg tablet twice/d)	20 mg daily (7–11 y old) (10 mg tablet twice a day)	For zafirlukast, administer at least 1 h before or 2 h after meals, to maximize bioavailability.
Zileuton	300 or 600 mg tablet	2,400 mg daily (give tablets 4 times/d)	—	With zileuton monitor hepatic enzyme alanine aminotransferase.
Methylxanthines				
Theophylline	Liquids, sustained-release tablets, and capsules	Starting dose 10 mg/kg/d up to 300 mg max; usual max 800 mg/d	Starting dose 10 mg/kg/d; usual max: < 1 y old: 0.2 (age in weeks) + 5 = mg/kg/d ≥ 1 y old: 16 mg/kg/d	Adjust dose to achieve serum concentration of 5–15 μg/mL at steady-state (at least 48 h on same dosage). Because of wide interpatient variability of theophylline metabolic clearance, routine serum theophylline level monitoring is important.

MDI = metered-dose inhaler.
DPI = dry-powder inhaler.
*Compare information on inhaled corticosteroids in Table 4.
†Children ≤ 12 y old.
(Adapted from Reference 3).

Table 4. Estimated Daily Doses for Inhaled Corticosteroids

Drug	Amount Delivered Per Puff (μg)	Low Daily Dose (μg)		Medium Daily Dose (μg)		High Daily Dose (μg)	
		Adult	Child*	Adult	Child*	Adult	Child*
Beclomethasone CFC	42 or 84	168–504	84–336	504–840	336–672	> 840	> 672
Beclomethasone HFA	40 or 80	80–240	80–160	240–480	160–320	> 480	> 320
Budesonide DPI	200	200–600	200–400	600–1,200	400–800	> 1,200	> 800
Flunisolide	250	500–1,000	500–750	1,000–2,000	1,000 –1,250	> 2,000	> 1,250
Fluticasone MDI	44, 110, or 220	88–264	88–176	264–660	176–440	> 660	> 440
Fluticasone DPI	50, 100, or 250	100–300	100–200	300–600	200–400	> 600	> 400
Triamcinolone acetonide	100	400–1,000	400–800	1,000–2,000	800–1,200	> 2,000	1,200

*Children ≤ 12 y old.
CFC = chlorofluorocarbon.
HFA = hydrofluoroalkane.
DPI = dry powder inhaler.
MDI = metered-dose inhaler.
NA = not applicable.
(Adapted from Reference 3).

Safety of Inhaled Corticosteroids

What are the adverse effects of long-term use of inhaled corticosteroids by children? Do they affect vertical growth or bone density? Do they have ocular toxicity? Do they suppress adrenal/pituitary function? Recently the American College of Chest Physicians and the American Academy of Allergy, Asthma, and Immunology convened an expert panel to address those questions.[7] That panel's systematic review came to the same conclusions as the NAEPP Expert Panel Report of 2002, which was that the asthma-control benefit of inhaled corticosteroids decidedly outweighs the risks from inhaled corticosteroids, and the NAEPP Expert Panel recommendations now reflect that finding (Tables 1-4).

The systematic review by Leone et al[7] found 2 randomized, blinded clinical trials that indicated that inhaled corticosteroids are not associated with lower bone density in asthmatic children. Among adults, generally, long-term use of inhaled corticosteroids is not associated with significantly lower bone density; however, patients who take high doses of inhaled corticosteroids for many years may suffer clinically important adverse effects.

Leone et al[7] found that inhaled corticosteroids are associated with a slower short-term vertical growth rate but that the overall effect is small and may not be sustained. They concluded that the adult height attained by asthmatic children treated with inhaled corticosteroids is not different from that of nonasthmatics. The NAEPP Expert Panel Report of 2002 came to a similar conclusion: inhaled corticosteroids may reduce vertical-growth velocity in children, but children whose asthma is inadequately controlled also suffer slower vertical growth.[3]

No high-level evidence indicates that low-to-medium-dose inhaled corticosteroids are associated with cataracts or glaucoma.[8] An Australian community-based study of 2,784 asthma patients found more cataracts among adult lifetime users of inhaled corticosteroids,[9] but that study may have been biased by missing data. In a multicenter, randomized trial of 384 patients Reed et al[10] found no higher risk of cataracts among users of inhaled corticosteroids. Studies of children who use inhaled corticosteroids drew the same conclusion about inhaled corticosteroids and cataracts.[11,12]

Low-to-medium doses of inhaled corticosteroids may cause clinically unimportant effects on hypothalamic-pituitary-adrenal function in children. This subject needs further research, especially with regard to pubescent asthmatic children.

Antibiotic Therapy

There is a dearth of high-level data on the value of antibiotics for managing asthma. There have been only 2 studies of antibiotic treatment of asthma,[13,14] Both of those studies are more than 20 years old and they had a total of only 121 participants. Thus, on this subject the NAEPP Expert Panel Report of 2002 was unchanged from the previous 2 versions: antibiotic therapy has no role in asthma management unless there a comorbidity such as pneumonia, fever with purulent sputum, or suspected bacterial sinusitis.[3] Further research is needed on the relationship between sinusitis and asthma exacerbation.

Asthma Action Plans

It has long been believed that asthma patients should have written asthma action plans as self-management tools, but do written asthma action plans improve outcomes? The NAEPP Expert Panel Report of 2002 concluded the existing data are insufficient to support or refute the benefits of written asthma

action plans, compared to usual medical management.[3] Seven studies (with a total of > 1,400 patients) were considered, but unfortunately none of them met the research-quality criteria to be included as evidence in the systematic review.[15–19] Thus, the NAEPP Expert Panel Report of 2002 recommends (as did the 1991 and 1997 versions) that asthma patients have written asthma action plans.[1–3] This is especially pertinent for those who have moderate or severe asthma or a history of severe asthma exacerbation. Clinicians should treat the written asthma action plan as part of the care plan. The written asthma action plan should provide clear, explicit, patient-specific information for environmental control and detailed steps to follow if the medications are ineffective or if for any other reason the patient has an asthma emergency. The plan should list contact people and/or organizations to call for immediate care. Further research is needed on how to maximize the effectiveness of written asthma action plans in school settings (including daycare and preschool), which plan formats are most effective, and how effective the plans are in the overall asthma management of children.

Should the Asthma Action Plan Be Based on Symptoms or on Peak Flow Monitoring?

There is inadequate evidence to determine whether the asthma action plan should be based on symptoms or on peak flow monitoring. The NAEPP Expert Panel Report of 2002 concludes that with patients who suffer moderate or severe asthma, peak flow monitoring should be considered.[3] Peak flow monitoring may enhance clinician-patient communication and increase patient and caregiver awareness of the asthma and asthma control.

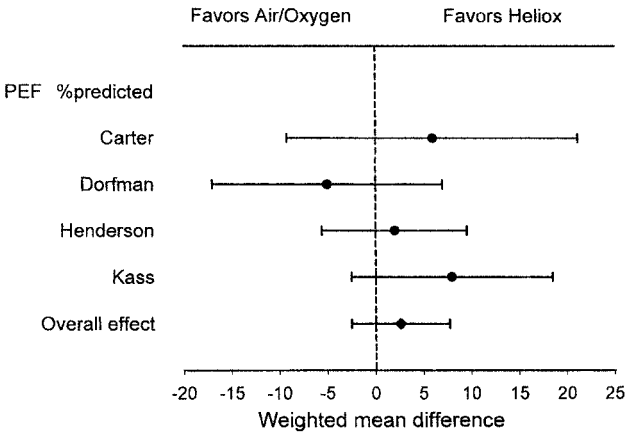

Fig. 1. Analysis of evidence on the effect of helium-oxygen mixture (heliox) (vs air/oxygen) on percent-of-predicted peak expiratory flow (PEF % predicted) from 5 studies. (From Reference 24, with permission).

Regarding whether to base the written asthma action plan on symptoms or on peak flow measurement, the literature review for the NAEPP Expert Panel Report of 2002 found only 4 studies that met the research-quality criteria to be included as evidence in the systematic review.[17,18,20,21] The panel recommended more research on the following questions: Is peak flow monitoring superior to symptom monitoring? Which patients are most likely to benefit from peak flow monitoring? Are there benefits from using a peak flow meter for ongoing monitoring? Is peak flow monitoring more likely to be used regularly, instead of only during exacerbations?[3]

Heliox

The earliest use of heliox was in 1935, as a treatment for upper and lower respiratory tract obstruction.[22] For asthma patients heliox decreases dyspnea and work of breathing.[23] Some centers use heliox as a rescue treatment for asthma.

In a systematic review Ho et al[24] reported that heliox may mildly-to-moderately benefit acute asthma within the first hour of use, but heliox is less advantageous after that first hour. They concluded that there are insufficient data on whether heliox can avert tracheal intubation or decrease hospital or intensive care admissions. Their systematic review identified 4 randomized controlled studies that had a common variable (peak expiratory flow) suitable for meta-analysis.[25–28] Those 4 studies combined yielded a 92% confidence interval that heliox offers a small benefit over air and oxygen, including slightly better improvement of dyspnea (Fig. 1). Heliox may temporize (during the first hour of an asthma exacerbation) before other medications are administered, and it may help avert intubation and mechanical ventilation. Of concern to Ho et al was the fact that in most of the trials there was no method to prevent entrainment of room air into the heliox nor was there compensation for the fact that heliox cannot nebulize liquid as well as oxygen or air.

Rodrigo et al[29] reviewed randomized and nonrandomized prospective, controlled trials (which included children and adults) and compared heliox to standard asthma therapy plus placebo. Seven trials were selected for inclusion, with a total of 392 acute-asthma patients.[26–28,30–33] The commonly measured outcomes in those trials were peak expiratory flow or FEV_1. There was no significant difference between the heliox group and the oxygen/air group. Rodrigo et al concluded that existing evidence does not support emergency-department use of heliox with patients suffering moderate-to-severe acute asthma (Figs. 2 and 3). Further study is needed on the application of heliox with pediatric patients and with patients who are already receiving inhaled corticosteroids. It would also be useful to determine whether heliox affects duration of stay or intubation rate.

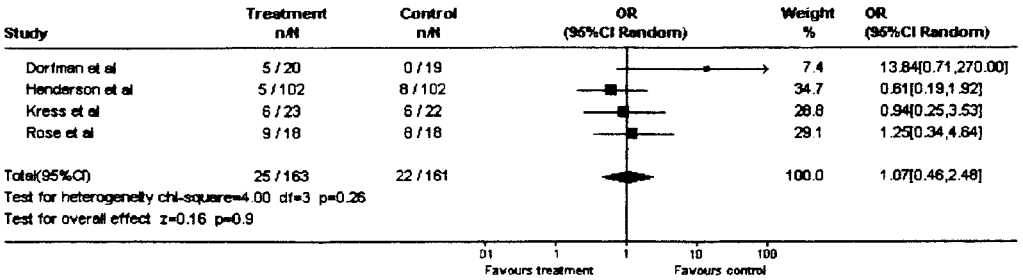

Fig. 2. Pooled odds ratios (OR, plotted on a logarithmic scale) of hospital admissions, comparing helium-oxygen mixture (heliox) (treatment group) to air/oxygen (control group). The horizontal lines are 95% confidence intervals around the point estimates (black squares), and the sizes of the black squares represent the relative weight of each trial in the pooled summary estimate (diamond). The vertical line represents the point of "no effect" (OR of 1.0). CI = confidence interval. (From Reference 29, with permission.)

Metered-Dose Inhaler Versus Other Aerosol Devices for β_2-Agonist Delivery

Metered-dose inhalers (MDIs) are commonly used in asthma management and they have several advantages over nebulizers. Ram et al comprehensively and systematically reviewed MDIs and other inhalation devices.[34] They selected 84 randomized controlled studies from MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and the Cochrane Airways Group specialized trials database. They found no significant differences between MDI and 13 other inhaler devices. The outcome measures included lung function, blood pressure, symptoms, bronchial hyperreactivity, inhaled steroid requirements, serum potassium, and use of additional relief bronchodilators. They found no evidence that MDIs are more or less effective than alternative inhaler devices for delivering long-acting B_2-agonist bronchodilators to asthma patients; MDIs (or the cheapest inhaler device) should be the first-line treatment in all stable-asthma patients who require B_2 agonists.

MDI Versus Other Aerosol Devices for Inhaled-Corticosteroids Delivery

Brocklebank et al systematically reviewed whether MDIs deliver inhaled corticosteroids more effectively than other inhalers.[35] The reports included in that review were from the Cochrane Airways Group trials, MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials. The review included 24 randomized, controlled studies, of both pediatric and adult stable asthmatics, and the studies compared MDIs to other inhaler devices (except nebulizers) that deliver inhaled corticosteroids. They found significant differences in $FEV_{1,}$ morning peak expiratory flow, and use of additional drugs among the patients who used dry-powder inhaler (vs other devices), but they also found that those differences were within clinically equivalent limits and that there were no significant differences when baseline characteristics were considered. They concluded that non-MDI devices are not more or less effective than MDI for administering inhaled cortico-

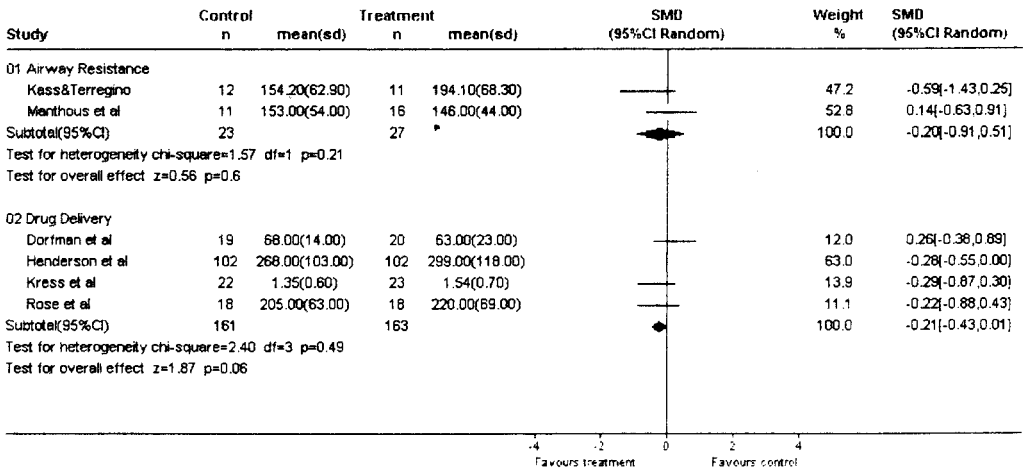

Fig. 3. Pooled standardized mean differences (SMD) in lung function, after treatment with inhaled heliox (treatment group) or oxygen/air (control group). SMD represents difference in means between groups displayed on standard deviation (SD) units. Width of horizontal line represents 95% confidence intervals (CI) around point estimate (gray square). Size of point estimate represents relative weight (percentage of weight) of each trial in the pooled summary estimate (diamond) (From Reference 29, with permission.).

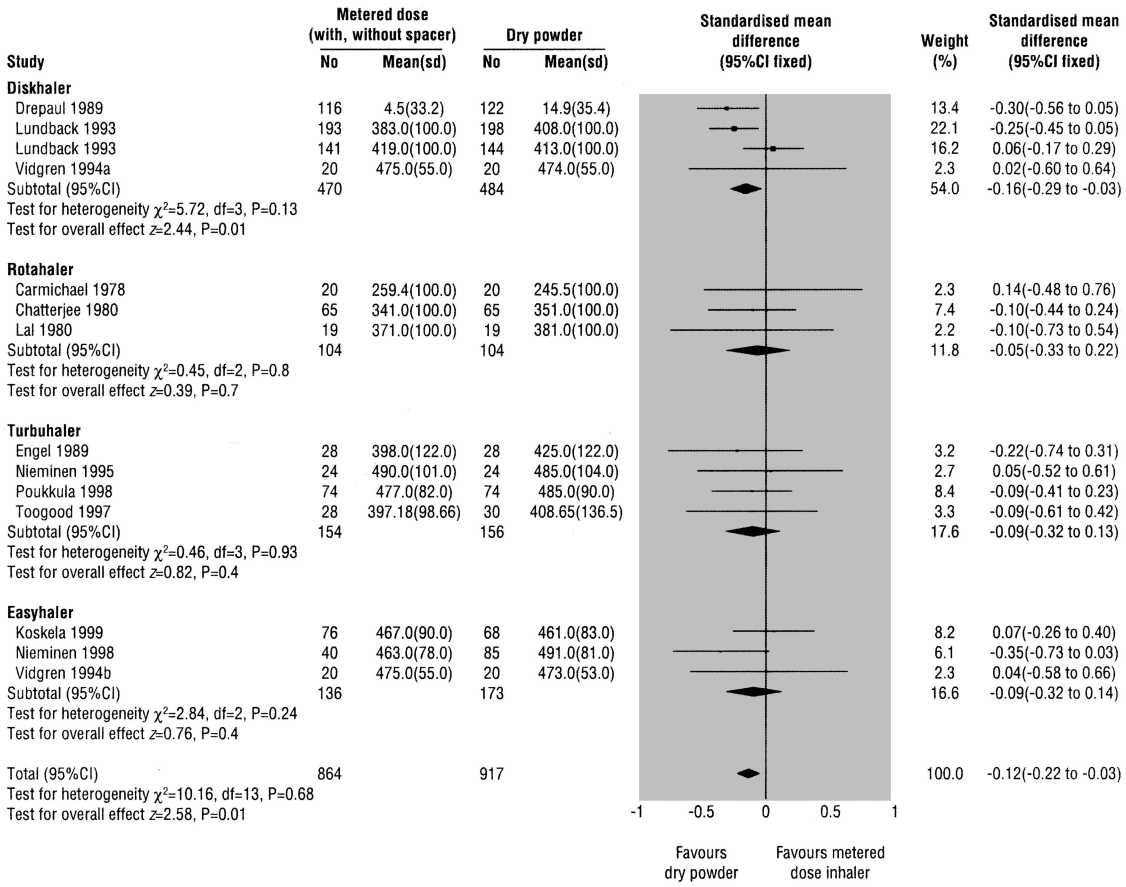

Fig. 4. Morning peak expiratory flow associated with treatment with metered-dose inhaler (with and without spacer) versus with 4 dry powder inhalers (Diskhaler, Rotohaler, Turbuhaler, and Easyhaler). CI = confidence interval. (From Reference 35, with permission.)

steroids, and so the least expensive delivery method (which at present is MDI) should be used (Fig. 4).

Summary: A Challenge for Respiratory Therapists

Respiratory therapists should help to advance medical science by always maintaining a high degree of suspicion regarding claims about both old and new health care devices, treatments, and methods. That healthy skepticism and demand for hard evidence are the heart of evidence-based medicine, and we should be ready to adopt (not resist) the practice changes that rigorous research will suggest. Some of our established practices and concepts of asthma management will not withstand the scrutiny of multicenter, properly powered, randomized controlled trials. Measuring and monitoring devices are also subject to reevaluation; some widely used devices might be less effective than we believe.

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