

Community-Engaged Scholarship to Catalyze Innovation: A Case Study of the Uptake of Metered-Dose Inhalers with Spacers to Deliver Respiratory Medication in a Pediatric Emergency Department in Nova Scotia

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Appendix 1: Nebulization versus metered-dose inhalers with spacers: β_2 Adrenergic receptor agonist delivery in wheezy pediatric patients: Key published reviews, clinical trials, surveys, and editorials, 1984 to 2010

Date	Authors	Title	Journal	Country	Design	N (age)	Conclusion(s)
1984	Frelander M, van Asperen PP	Nebuhaler versus nebuliser in children with acute asthma.	<i>British Medical Journal (Clinical Research Edition)</i> , Vol. 288, No. 6434 (Jun. 23, 1984), pp. 1873-1874.	Australia	Randomized trial	28 (3–13 years)	"...in children with acute asthma equal bronchodilatation can be achieved with Nebuhalers and nebulisers."
1986	Fuglsang G, Pedersen S	Comparison of Nebuhaler and nebulizer treatment of acute severe asthma in children.	<i>Eur J Respir Dis.</i> 1986 Aug;69(2):109-13.	Denmark	Randomized double-blind cross-over trial	21 (7–14 years)	"...children with acute severe asthma were treated with terbutaline delivered by a pressurized aerosol with a ... spacer (Nebuhaler) or as a nebulized solution ... nebuhaler treatment resulted in significantly greater bronchodilation than treatment with the nebulizer."
1989	Ba M, Spier S, Lapierre G, Lamarre A	Wet nebulizer versus spacer and metered dose inhaler via tidal breathing.	<i>J Asthma.</i> 1989;26(6):355-8.	Canada	Randomized, double-blind trial	27 (7–18 years)	"The [MDIs] technique seems to have several practical advantages over [nebulization]. ...We conclude that the very simple and time-saving technique of tidal breathing using a [MDIs] is a very practical method for delivering beta2- adrenergic medicines in the older hospitalized child (aged 7–18) with acute moderately severe asthma and achieves at least as good bronchodilatation as the standard wet nebulization of the medication."

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1989	Benton G, Thomas RC, Nickerson BG, et al.	Experience with a metered-dose inhaler with a spacer in the pediatric emergency department.	<i>Am J Dis Child.</i> 1989 Jun;143(6):678-81.	US	Non-randomized trial	13 (1–13 years)	"[MDIs] are an effective device for the treatment of asthma in paediatric ED..."
1989	Conner WT, Dolovich MB, Frame RA, Newhouse MT	Reliable salbutamol administered in 6- to 36-month-old by means of a metered dose inhaler and aerochamber with mask.*	<i>Pediatr Pulmonol.</i> 1989;6(4):263-7.	Canada	Double-blind trial	NA (6–36 months)	"The MDI and Aerochamber with mask is an effective delivery system for respiratory therapy in these young children."
1989	Nosedá A, Yernault JS	Sympathomimetics in acute severe asthma: inhaled or parenteral, nebulizer or spacer?	<i>Eur Respir J.</i> 1989 Apr;2(4):377-82.	Belgium	Review	NA	"The conventional mode of inhalation therapy in acute asthma is nebulization, but equally effective bronchodilatation may be obtained with [MDIs]."
1989	Pendergast J, Hopkins J, Timms B, Van Asperen PP	Comparative efficacy of terbutaline administered by Nebuhaler and by nebulizer in young children with acute asthma.*	<i>Med J Aust.</i> 1989 Oct 2;151(7):406-08.	Australia	NA	27 (3–6 years)	"The decline [in baseline clinical score] that was achieved with delivery of the drug by way of a Nebuhaler ...was not significantly different from that with a nebulizer..."
1991	Lee N, Racheletsky G, Kobayashi RH, et al	Comparison of efficacy and safety of albuterol administered by power-driven nebulizer (PDN) versus metered-dose inhaler (MDI) with Aerochamber and mask in young children with asthma.	<i>J Allergy Clin Immunol</i> 1991 Jan; 87(1): 307.	US	Randomized double-blind, double-dummy trial	33 (0.5–5 years)	"...[Salbutamol] treatment... with Aerochamber plus mask is as effective and safe as ...[delivery by] power-driven nebulizer for acute asthmatic attacks in children."

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1991	Newhouse M	Advantages of pressurized canister metered dose inhalers.	<i>J Aerosol Med.</i> 1991 Fall;4(3):139-50.	Canada	Review	NA	"While nebulizers and powder inhalers both have an important role to play in the management of airway and parenchymal disease, there is, as yet, no all-purpose aerosol generation and delivery system to replace the MDI."
1992	Vazquez Cordero C, Corera Sanchez M, Molinuevo Alvaro J	[Comparison of treatment of acute asthma attacks in children with salbutamol dispensed by the Volumatic dispenser or by a nebulizer.]	<i>An Esp Pediatr.</i> 1992 May;36(5):359-62.	Spain	Comparative trial	18 (NA)	"Treatment of acute asthma in children with salbutamol via [MDIs] and tidal breathing mechanism may be an efficacious, safe and readily available method..."
1993	Idris AH, McDermott MF, Raucci JC et al.	Emergency department treatment of severe asthma: Metered-dose inhaler plus holding chamber is equivalent in effectiveness to nebulizer.	<i>Chest.</i> 1993 Mar;103(3):665-72.	US	Randomized, double-blind, placebo-controlled intervention trial	35 (10-45 years)	"When compared with nebulizer, the [MDIs] delivers a full dose of [salbutamol] more quickly and at no higher cost."
1993	Kerem E, Levison H, Schuh S et al.	Efficacy of albuterol administered by nebulizer versus spacer device in children with acute asthma.	<i>J Pediatr.</i> 1993 Aug;123(2):313-7.	Canada	Randomized double-blind trial	33 (6-14 years)	"...[MDIs] and nebulizers are equally effective means of delivering beta 2-agonists to children with acute asthma."
1994	Chiaretti A, Pullano A, Drigo L et al.	[The use of spacer devices as an innovative approach in the treatment of asthma].	<i>Pediatr Med Chir.</i> 1994 May-Jun;16(3):255-60.	Italy	Comparative trial	NA	"Our data seem to encourage the use of [MDIs] in childhood asthma for the real better effectiveness and for the reduced rate and severity of systemic effects of inhaled drugs."

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1994	Cunningham SJ, Crain EF	Reduction of morbidity in asthmatic children given a spacer device.	<i>Chest</i> . 1994 Sep;106(3):753-7.	US	Randomized controlled trial	84 (3–10 years)	“Introducing [MDIs] to patients in a busy, inner-city pediatric ED is an effective and efficient intervention that improves the functioning of asthmatic children in terms of resolution of cough and wheeze and school absenteeism.”
1995	Chou KJ, Cunningham SJ, Crain EF	Metered-dose inhalers with spacers vs nebulizers for pediatric asthma.	<i>Arch Pediatr Adolesc Med</i> . 1995 Feb;149(2):201-5.	US	Randomized trial with two arms	152 (>2 years)	“There were no ... differences between the groups in outcomes... Patients given MDIs ... required shorter treatment times in the ED (66 minutes vs 103 minutes, $P < .001$). Fewer patients in the spacer group had episodes of vomiting in the ED (9% vs 20%, $P < .04$), and patients in the nebulizer group had a significantly greater mean percent increase in heart rate from baseline to final disposition (15% vs 5%, $P < .001$). These data suggest that MDIs ... may be an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the ED.”
1995	Lin YZ, Hsieh KH	Metered-dose inhaler and nebulizer in acute asthma.	<i>Arch Dis Child</i> . 1995 Mar; 72(3): 214–218.	Taiwan	Randomized trial with two arms	111 (5–16 years)	“...[MDIs] in this study is superior to nebulizer treatment in terms of [oxygen saturation] and some spirometric measurements.”
1995	Parkin PC, Saunders NR, Diamond SA, Winders PM, Macarthur C	Randomized trial spacer v nebulizer for acute asthma.	<i>Arch Dis Child</i> . 1995 Mar;72(3):239-40.	Canada	Randomized, single-blind trial with two arms	60 (1–5 years)	“...[MDIs] is an effective delivery method for young hospitalized asthmatic children.”
1996	Williams JR, Bothner JP, Swanton RD	Delivery of albuterol in a pediatric emergency department.	<i>Pediatr Emerg Care</i> . 1996 Aug;12(4):263-7.	US	Randomized trial with three arms	60 (6–18 years)	“In a pediatric [ED] setting, aerosolized [salbutamol] delivered by [MDIs] was equal in effectiveness to nebulization in the acute asthma management of children \geq six years of age.”

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1997	Amirav I, Newhouse MT	Metered-dose inhaler accessory devices in acute asthma: efficacy and comparison with nebulizers: a literature review.	<i>Arch Pediatr Adolesc Med.</i> 1997 Sep;151(9):876-82.	US	Review (1980–1996)	552 (0.5–18 years)	"[MDIs] should be considered the preferred mode of treatment of children with acute asthma."
1997	Batra V, Sethi GR, Sachdev HP	Comparative efficacy of jet nebulizer and metered dose inhaler with spacer device in the treatment of acute asthma.	<i>Indian Pediatr.</i> 1997 Jun;34(6):497-503.	India	Randomized prospective trial	60 (1–12 years)	"[MDIs] is as effective as a nebulizer for the aerosolized administration of salbutamol in an acute exacerbation of asthma in children in the ED...for developing countries, distinct advantages (economic and power requirement) argue strongly for utilization of [MDIs] in preference to nebulizer."
1997	Gappa M, Gärtner M, Poets CF, von der Hardt H	Effects of salbutamol delivery from a metered dose inhaler versus jet nebulizer on dynamic lung mechanics in very preterm infants with chronic lung disease.	<i>Pediatr Pulmonol.</i> 1997 Jun;23(6):442-8.	Germany	Clinical trial	13 (37 weeks)	"...[MDIs] improves dynamic resistance as effectively as...jet nebulizer and may therefore be a preferable mode of aerosol administration [in small preterm infants]."
1998	Closa RM, Ceballos JM, Gómez-Papí A et al.	Efficacy of bronchodilators administered by nebulizers versus spacer devices in infants with acute wheezing.	<i>Pediatr Pulmonol.</i> 1998 Nov;26(5):344-8.	Spain	Randomized double-blind trial	34 (1–24 months)	"...MDIs and nebulizers are equally effective means of delivering beta-2 agonists to infants and small children with acute wheezing."
1998	Robertson CF, Norden MA, Fitzgerald DA et al.	Treatment of acute asthma: salbutamol via jet nebuliser vs spacer and metered dose inhaler.	<i>J Paediatr Child Health.</i> 1998 Apr;34(2):142-6.	Australia	Randomized double-blind parallel design trial	155 (4–12 years)	"Administration of salbutamol via a [MDIs] provides effective relief in the management of acute asthma in children, but to a lesser extent than a jet nebuliser."

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1999	Dewar AL, Stewart A, Cogswell JJ, Connett GJ	A randomised controlled trial to assess the relative benefits of large volume spacers and nebulisers to treat acute asthma in hospital.	<i>Arch Dis Child.</i> 1999 May;80(5):421-3.	UK	Randomized controlled trial	61 (>3 years)	"[MDIs] are an acceptable, cost effective alternative to nebulisers in ...children admitted with acute asthma, provided that the children can use the mouthpiece, and symptoms are not severe. Their use facilitates effective home treatment by parents with subsequent reduction in morbidity and re-admission rates."
1999	Melnyk B	Building a case for evidence-based practice: Inhalers vs. nebulizers.	<i>Pediatr Nurs.</i> 1999 Jan-Feb;25(1):102-3.	US	Review	NA	"Because many parents and health care providers are intuitively convinced that nebulizers provide additional therapeutic benefits, it may be a challenging endeavor to influence this change in practice for children experiencing acute exacerbations of asthma. Even with older school-age children and adolescents, spacers improve the delivery of bronchodilator medication into the airways and minimize the amount of medication deposited in the mouth and throat. Therefore, they should be used routinely with children of all ages."
1999	Newhouse M	Asthma therapy with aerosols: Are nebulizers obsolete? A continuing controversy.	<i>J Pediatr.</i> 1999 Jul;135(1):5-8.	Canada	Editorial	NA	"In medical practice, despite the increasing acceptance of "evidence-based" therapeutics, the "tried and true" may persist long after the evidence is overwhelmingly in favor of change."
1999	Schuh S, Johnson D, Stephens D et al.	Comparison of albuterol delivered by a metered dose inhaler with spacer versus a nebulizer in children with mild acute asthma.	<i>J Pediatr.</i> 1999 Jul;135(1):22-7.	Canada	Randomized double-blind trial	90 (5-17 years)	"In children with mild acute asthma, treatment with... [salbutamol] by an [MDIs] is just as clinically beneficial as treatment with higher doses delivered by an MDI or by a nebulizer."

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1999	Valencia ML, Manotas R	Inhaled vs nebulised salbutamol in the management of acute asthma exacerbation in pre-school children.	<i>latreia</i> . 1999;12(3):130-04.	Columbia	Randomized comparative trial	70 (1–6 years)	“...results of treatment of acute asthma crises were similar regardless of the system of administration of salbutamol, either inhaled or nebulized.”
1999	Wildhaber JH, Dore ND, Wilson JM, Devadason SG, LeSouref PN	Inhalation therapy in asthma: nebulizer or pressurized metered-dose inhaler with holding chamber? In vivo comparison of lung deposition in children.	<i>J Pediatr</i> . 1999 Jul;135(1):28-33.	Australia	Clinical trial	17 (2–9 years)	“For the same age groups we have shown equivalent percentages of total lung deposition of radiolabeled salbutamol aerosolized by either a nebulizer or a [MDIs].”
2000	Callahan CW	Wet nebulization in acute asthma: The last refrain?	<i>Chest</i> . 2000;117(5): 1226-1228. doi:10.1378/chest.117.5.1226.	US	Editorial		“There is... both clinical and physiologic evidence to support the use of MDI therapy in place of nebulization. Why is this idea met with incredulous stares by clinicians, as it was when I suggested it recently at our department’s morning report? Old therapies, it seems, tend to linger in the mind in much the same way as old melodies.”
2000	Leversha AM, Campanella SG, Aickin RP, Asher MI	Costs and effectiveness of spacer versus nebulizer in young children with moderate and severe acute asthma.	<i>J Pediatr</i> . 2000 Apr;136(4):497-502.	New Zealand	Randomized, double-blind, placebo-controlled trial	60 (1–4 years)	“[MDIs] was a cost-effective alternative to a nebulizer in the delivery of [salbutamol] to young children with moderate to severe acute asthma.”
2000	Mandelberg A, Tseheri S, Houris S et al.	Is nebulized aerosol treatment necessary in the pediatric emergency department?	<i>Chest</i> . 2000 May;117(5):1309-13.	Israel	Randomized, double-blind, placebo-controlled trial	42 (1–4 years)	“...even in the group of unselected very young children... the use of [MDIs] is at least as effective as the use of [a nebulizer].”

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2000	Ploin D, Chapuis FR, Stamm D et al.	High-dose albuterol by metered-dose inhaler plus a spacer device versus nebulization in preschool children with recurrent wheezing: A double-blind, randomized equivalence trial.	<i>Pediatrics</i> . 2000 Aug;106(2 Pt 1):311-7.	France	Randomized double-blind parallel group equivalence trial	64 (1–5 years)	“The efficacy of [salbutamol] administered using the spacer device was equivalent to that of the nebulizer. Given its high tolerance, repeated 50-microg/kg doses of [salbutamol] administered through the spacer device should be considered in hospital emergency departments as first-line therapy for wheezing.”
2000	Rubilar L, Castro-Rodriguez J, Girardi G	Randomized trial of salbutamol via metered-dose inhaler with spacer versus nebulizer for acute wheezing in children less than 2 years of age.	<i>Pediatr Pulmonol</i> . 2000 Apr;29(4):264-9.	Chile	Randomized, single-blind trial	123 (1–24 months)	“...in this study population, children less than 2 years of age with moderate-severe exacerbations of wheezing responded faster to salbutamol delivered by [MDIs] (with a facial mask) than to salbutamol delivered by nebulizer.”
2001	Al-Sallami H, Ball P, Davey A	Metered-dose inhaler with spacer versus nebuliser for acute exacerbation of asthma - a literature review.	<i>Aust J Hosp Pharm</i> 2001;31(3):179–250.	Australia	Review (1970–2000)	2310 (NA – 1681 children included)	Conclusions re children and infants: MDIs were as effective or more effective than nebulisers. Three studies found that MDIs were more acceptable to patients than nebulizers. One study found that a MDIs device provided less relief than a nebuliser.
2001	Gazarian M, Henry R, Wales S et al.	Evaluating the effectiveness of evidence-based guidelines for the use of spacer devices in children with acute asthma.*	<i>Med J Aust</i> . 2001 Apr 16;174(8):394-7.	Australia	Before-after trial	247 (NA)	The authors report on a clinical change in children presenting to the ED with mild to moderate acute asthma - from nebulizers to MDIs. They found no change in admission rates or length of stay in hospital following admission.
2001	Powell C, Maskell G, Marks M et al.	Successful implementation of spacer treatment guideline for acute asthma.	<i>Arch Dis Child</i> . 2001 Feb; 84(2): 142–146.	Australia	Before-after trial	191 (NA)	“...implementation of a new evidence based guideline can be achieved using specific strategies for promoting the application of research findings in the clinical arena.”

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2001	Tien I, Dorfman D, Kastner B, Baucher H	Metered-dose inhaler: the emergency department orphan.	<i>Arch Pediatr Adolesc Med.</i> 2001 Dec;155(12): 1335-9.	US	Mail survey	333	"Misconceptions regarding the efficacy and safety of [MDIs] for the treatment of acute asthma exacerbations exist but are limited to a minority of surveyed emergency medicine physicians caring for children. Nebulizers remain the preferred method of routine bronchodilator delivery by physicians providing care to pediatric asthmatics in the emergency department."
2002	Buxton LJ, Baldwin JH, Berry JA, Mandelco BL	The efficacy of metered-dose inhalers with a spacer device in the pediatric setting.	<i>J Am Acad Nurse Pract.</i> 2002 Sep;14(9):390-7.	US	Systematic review	NA (NA)	"No significant difference between the [MDIs] and nebulizer in delivering medication in an acute exacerbation of asthma was found in this analysis. The practitioner's choice of delivery methods should reflect the family's preference, the practice situation, and economic considerations."
2002	Cotterell EM, Gazarian M, Henry RL, O'Meara MW, Wales SR	Child and patient satisfaction with the use of spacer devices in acute asthma.	<i>J Paediatr Child Health.</i> 2002 Dec;38(6):604-7.	Australia	Survey	111	"The use of spacer devices in mild to moderately severe acute asthma is highly acceptable for children and parents; the majority prefer this mode of drug delivery to nebulization."
2002	Duarte M, Camargos P	Efficacy and safety of a home-made non-valved spacer for bronchodilator therapy in acute asthma.	<i>Acta Paediatr.</i> 2002;91(9):909-13.	Brazil	Randomized trial	196 (4-15 years)	"...comparable efficacy in mild to moderate acute asthma... The frequency of side effects was significantly higher in the [nebuliser] group than in the [MDI with an alternative home-made non-valved spacer] group."
2002	Zar HJ, Asmus MJ, Weinberg EG	A 500-ml plastic bottle: An effective spacer for children with asthma.	<i>Pediatr Allergy Immunol.</i> 2002 Jun;13(3):217-22.	South Africa	Review	NA	"...a modified 500-ml plastic bottle is an effective spacer; modification and use of this device should be included in international guidelines for the management of children with asthma."

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2003	Delgado A, Chou KJ, Silver EJ, Crain EF	Nebulizers vs metered-dose inhalers with spacers for bronchodilator therapy to treat wheezing in children aged 2 to 24 months in a pediatric emergency department.	<i>Arch Pediatr Adolesc Med.</i> 2003 Jan;157(1):76-80.	US	Randomized, double-blind, placebo-controlled trial	168 (2 -24 months)	"...[MDIs] may be as efficacious as nebulizers for the treatment of wheezing in children aged 2 years or younger."
2003	Vilarinho LC, Cardeal Mendes CM, Souza LS	[Metered-dose inhalers with home-made spacers versus nebulizers to treat moderate wheezing attacks in children].	<i>J Pediatr (Rio J).</i> 2003 Sep-Oct;79(5):403-12.	Brazil	Randomized, single-blind trial	54 (22 days–11 years)	"The home-made spacer with a metered-dose inhaler is a cost-effective alternative to a jet nebulizer to children with moderate wheezing attacks."
2004	Benito-Fernández J, González-Balenciaga M, Capapé-Zache S, Vázquez-Ronco MA, Mintegi-Raso S	Salbutamol via metered-dose inhaler with spacer versus nebulization for acute treatment of pediatric asthma in the emergency department.	<i>Pediatr Emerg Care.</i> 2004 Oct;20(10):656-9.	Spain	Clinical trial	580 (under 14 years)	"The administration of bronchodilators using [MDIs] is an effective alternative to nebulizers for the treatment of children with acute asthma exacerbations in the emergency department."
2004	Castro-Rodríguez JA, Rodrigo GJ	β -agonists through metered-dose inhaler with valved holding chamber versus nebulizer for acute exacerbation of wheezing or asthma in children under 5 years of age: a systematic review with meta-analysis.	<i>J Pediatr.</i> 2004 Aug;145(2):172-7.	Chile	Systematic review with meta-analysis	491 (under 5 years)	"The use of an [MDIs] was more effective in terms of decreasing hospitalization and improving clinical score than the use of a nebulizer in the delivery of beta-agonists to children under 5 years of age with moderate to severe acute exacerbations of wheezing or asthma."

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2005	Boyd R, Stuart P	Pressurised metered dose inhalers with spacers versus nebulisers for beta-agonist delivery in acute asthma in children in the emergency department.	<i>Emerg Med J.</i> 2005 Sep;22(9):641-2.	Australia	Before-after trial	350 (NA)	"Introduction of routine [MDIs] treatment in the paediatric ED results in a significant drop in admission rates but no significant change in total hospital times or total ED times."
2005	Chong Neto HJ, Chong-Silva DC, Marani DM, et al.	Different inhaler devices in acute asthma attacks: a randomized, double-blind, placebo-controlled study.	<i>J Pediatr (Rio J).</i> 2005 Jul-Aug;81(4):298-304.	Brazil	Randomized, double-blind, placebo-controlled trial	40 (NA)	"The nebulizer was more expensive and used more medicine, showing the same efficiency. The homemade spacer was cheaper, but presented more side effects. The commercially available spacer was as expensive as the nebulizer, although safer. The dry powder inhaler was cheaper, but, just as the homemade spacer, it also caused tachycardia."
2005	Deerojanawong J, Manuyakorn W, Prapphal N et al.	Randomized controlled trial of salbutamol aerosol therapy via metered dose inhaler-spacer vs jet nebulizer in young children with wheezing.	<i>Pediatr Pulmonol.</i> 2005 May;39(5):466-72.	Thailand	Randomized, double-blind, placebo-controlled trial	47 (NA)	"...the efficacy of salbutamol aerosol therapy via [MDIs] compared to jet nebulizer in young wheezing children was not different in terms of clinical score and post-bronchodilator pulmonary function parameters. However, salbutamol aerosol therapy via jet nebulizer significantly increased the heart rate when compared to the [MDIs]."
2006	Cates C, Crilly JA, Rowe BH	Holding chambers (spacers) vs nebulisers for beta-agonist treatment of acute asthma.	<i>Cochrane Database of Systematic Reviews</i> 2006, Issue 2. Art. No.: CD000052. DOI 10.1002/14651858.CD000052.pub2. ⁵	UK	Systematic Review	2909 (2295 children and 614 adults) as of Jan 2008 update	"Nebuliser delivery produced outcomes that were not significantly better than MDIs in adults or children, in trials where treatments were repeated and titrated to the response of the participant. Spacers may have some advantages compared to nebulisers for children with acute asthma."

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2006	Jamalvi SW, Raza SJ, Naz F, Shamim S, Jamalvi SM	Management of acute asthma in children using metered dose inhaler and small volume nebulizer.	<i>J Pak Med Assoc.</i> 2006 Dec;56(12):595-9.	Pakistan	Randomized controlled trial	150 (0.5–15 years)	"...[MDIs] is an effective alternative to nebulizer for the treatment of children with acute asthma exacerbation in the ER."
2006	McVeen V, Mehdi N	Survey of albuterol delivery methods in emergency departments for acute asthma exacerbation in children 2 months to 15 years.	<i>Pediatr Asthma Allergy Immunol</i> 2006; 19[3]:180–184).	US	Survey	NA	A survey of emergency program directors found the use of MDIs for acute asthma exacerbation is 'seldom used'.
2006	Sannier N, Timsit S, Cojocaru B et al.	[Metered-dose inhaler with spacer vs nebulization for severe and potentially severe acute treatment in the pediatric emergency department].	<i>Arch Pediatr.</i> 2006 Mar;13(3):238-44.	France	Randomized trial	79 (4-15 years)	"The administration of beta 2 agonist using a [MDIs] is an effective alternative to nebulizers for the treatment of children with severe or potentially severe acute asthma in the emergency department."
2007	Norton SP, Pusic MV, Taha F, Heathcote S, Carleton BC	Effect of a clinical pathway on the hospitalization rates of children with asthma: a prospective study.	<i>Arch Dis Child.</i> 2007 Jan; 92(1): 60–66.	Canada	Before–after, controlled trial	267 (1-18 years)	"An evidence based clinical pathway for children and adolescents with moderate to severe exacerbations of acute asthma markedly decreases their rate of hospitalisation without increased return to emergency care."
2008	Mason N, Roberts N, Yard N, Partridge MR	Nebulisers or spacers for the administration of bronchodilators to those with asthma attending emergency departments?	<i>Respir Med.</i> 2008 Jul;102(7):993-8. doi: 10.1016/j.rmed.2008.02.009.	UK	Survey, Time and motion trial, Intervention		"[MDIs] administration of bronchodilators to those with asthma attending EDs utilises less treatment time than use of a nebuliser. A survey of EDs in Greater London has shown that despite guideline conclusions there appears to be little evidence of reduction in use of nebulisers; a fear that use of alternatives might take nurses longer is not supported by this study."

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2008	Mathew JL, Singh M	Metered-dose inhaler with spacer in children with acute asthma.	<i>Indian Pediatr.</i> 2008 Apr;45(4):295-7.	India	Review	NA	"In acute asthma, bronchodilator delivery through [MDIs] is comparable, but not superior to nebulizer in terms of clinical response and adverse events. These results cannot be directly applied to children less than two years and those with life-threatening acute exacerbations for want of adequate data. There is no evidence on the impact of these delivery modes on convenience, incidence of infection and cost of therapy."
2008	Rodriguez-Martinez CE, Sossa M, Lozano JM	Commercial versus home-made spacers in delivering bronchodilator therapy for acute therapy in children.	<i>Cochrane Database Syst Rev.</i> 2008 Apr 16;(2):CD005536. doi: 10.1002/14651858.CD005536.pub2.	Columbia	Systematic review	658 (under 18 years)	"The aim of this review was to compare the response to inhaled beta-2 agonists delivered through MDI using home-made spacers to [MDI with two types of commercial spacers] in children with acute exacerbations of wheezing or asthma...This review... did not identify a difference between the three methods of delivering bronchodilator. The possible need for a face-mask in young children using home-made spacers should also be considered..."
2008	Vangveeravong M	A comparative study of efficacy of salbutamol via metered dose inhaler with volumatic spacer and via dry powder inhaler, easyhaler, to nebulization in mild to moderate severity acute asthma exacerbation in childhood.	<i>J Med Assoc Thai.</i> 2008 Oct;91 Suppl 3:S115-23.	Thailand	Randomized controlled trial	54 (5-18 years)	"Rapid-acting inhaled beta-2 agonist via [MDIs] can be used effectively compared with nebulization form in treating mild to moderate degrees of acute exacerbation of asthma in children with comparable side effects."

Date	Authors	Title	Journal	Country	Design	N (age)	Conclusion(s)
2009	Hussain-Rizvi A, Kunkov S, Crain E	Does parental involvement in pediatric emergency department asthma treatment affect home management?	<i>J Asthma</i> . 2009 Oct;46(8):792-5.	US	Randomized trial	86 (1-5 years)	"...children in the MDIs group were 7.5 times more likely to be using the MDIs for their [salbutamol] treatments (95%CI 1.6-35.6). Involving parents in treatment of asthma exacerbations in the ED using an MDIs may improve adherence to MDIs use at home."
2010	Clark NM, Houle C, Partridge MR, Leo HL, Paton JY	The puzzle of continued use of nebulized therapy by those with asthma.	<i>Chron Respir Dis</i> . 2010;7(1):3-7. doi:10.1177/1479972309357496.	UK/US	Editorial		"Although change in clinical behavior may be occurring, it is slow in coming. Asthma treatment continues to be hampered by a practice that doesn't deliver in the way that patients deserve."
2010	Kaashmiri M, Shepard J, Goodman B et al.	Repeat dosing of albuterol via metered-dose inhaler in infants with acute obstructive airway disease: A randomized controlled safety trial.	<i>Pediatr Emerg Care</i> . 2010 Mar;26(3):197-202. doi: 10.1097/PEC.0b013e3181d1e40d.	US	Randomized double-blind parallel design multicenter trial	87 (under 2 years)	"Cumulative dosing with [salbutamol]... via [MDIs] and face mask in children younger than 2 years did not result in any significant safety issues and improved [asthma symptom scores] by at least 48%."

MDIs = metered-dose inhaler with spacer; NA = not available; [] = Abstract only, article not available in English.

* = Abstract only available.

[§]Version 1: CJ Cates, A Bara, JA Crilly, BH Rowe. Holding chambers versus nebulisers for beta-agonist treatment of acute asthma. Article first published online: 22 Apr 2003 | doi:10.1002/14651858.CD000052.

Version 2: CJ Cates, JA Crilly, BH Rowe. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Article first published online: 19 Apr 2006 | doi:10.1002/14651858.CD000052.pub2.

Version 3: CJ Cates, EJ Welsh, BH Rowe. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Article first published online: 13 Sep 2013 | doi:10.1002/14651858.CD000052.pub3.