OPEN ACCESS

Inhaled salbutamol delivery in small children with disposable and reusable spacers: an in vitro study

Laura Ojanperä ,[1] Lauri Lehtimäki ,[1,2] Balázs Kelemen,[1] Peter Csonka [1]

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/archdischild-2025-328830).

[1]Tampere Universities, Tampere, Pirkanmaa, Finland
[2]Tampere University Hospital, Tampere, Finland

Correspondence to
Dr Peter Csonka; peter.csonka@tuni.fi

Received 17 March 2025
Accepted 2 August 2025

Check for updates

To cite: Ojanperä L, Lehtimäki L, Kelemen B, *et al*. *Arch Dis Child* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/archdischild-2025-328830

ABSTRACT

Background Research on spacers for paediatric breathing patterns is limited, especially for disposable types, which may be a practical alternative to reusable valved holding chambers (VHC) in certain clinical settings.

Methods In vitro, the fine particle dose (FPD) of salbutamol from a pressurised metered-dose inhaler (pMDI) was tested using two paperboard spacers—DispozABLE (Diz) and LiteAire (LA)—and three reusable VHCs: AeroChamber Plus Flow-Vu (AC), EasyChamber (EC) and OptiChamber Diamond (OC). The pMDI+VHC setup was connected to a child throat model without a facemask. Salbutamol availability for inhalation was measured using a Next Generation Impactor under three paediatric breathing patterns: calm breathing (6 and 4 year olds) and obstructive breathing.

Results Median FPD in the respirable range (1–5 µm) was significantly higher for EC compared with LA, Diz and AC. Obstructive breathing increased throat deposition for all spacers, with Diz showing the highest. LA had the lowest throat deposition in calm breathing, and EC in obstructive breathing.

Conclusion Traditional VHCs, especially EC and OC, outperformed disposable spacers. Among disposables, the valved LA performed better than the valveless Diz and may offer a cost-effective, practical alternative to reusable spacers in specific scenarios.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Short-acting β2-agonists delivered via pressurised metered-dose inhalers with valved holding chambers (VHCs) are the preferred treatment for acute wheezing in young children.

⇒ Disposable spacers offer a potentially cost-effective and hygienic alternative to reusable VHCs in emergency settings, but data on their performance remain scarce.

⇒ Prior studies suggest that different spacers can significantly vary in drug delivery efficiency, and findings from one spacer cannot be extrapolated to another.

WHAT THIS STUDY ADDS

⇒ Fine particle dose delivery was significantly higher with EasyChamber (EC) compared with all other spacers, including disposable models.

⇒ Among disposable spacers, the valved LiteAire (LA) performed better than the valveless DispoZABLE (Diz) and had comparable performance to some reusable VHCs in certain scenarios.

⇒ Obstructive breathing patterns increased throat deposition across all spacers, with the highest levels observed for Diz, reinforcing that the use of valveless design is not justified.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings reinforce the importance of selecting the most effective VHC, when possible, as performance varies significantly between devices.

⇒ While disposable spacers are not a substitute for high-performing VHCs such as EC, valved disposable options such as LA may be viable in settings where cleaning and reuse are impractical.

⇒ Policymakers and clinicians should consider both drug delivery efficiency and cost-effectiveness when integrating disposable spacers into acute care protocols, particularly for emergency and ambulatory settings.

INTRODUCTION

Acute wheezing, whether viral or asthma related, accounts for approximately 10% of emergency room (ER) visits in children, with hospitalisation required in 30–50% of cases.[1–3] In young children with acute wheeze, short-acting β2-agonists are commonly used for rapid symptom relief, particularly in emergency settings, although guideline recommendations differ by age group and clinical context.[4 5] For young children unable to use dry powder inhalers, international guidelines strongly recommend using pressurised metered-dose inhalers (pMDIs) with a valved holding chamber (VHC) over nebulisers in mild and moderate bronchoconstriction.[4 5]

Disposable or single-use spacers present a potentially viable alternative to reusable VHCs, particularly in emergency settings and lung function tests (eg, bronchodilator responsiveness testing). They may offer a convenient, hygienic and cost-effective solution, with unit prices ranging from one-fourth to one-tenth of reusable spacers. Disposable spacers vary in design and usability. They are commonly made of cardboard, sometimes incorporating plastic elements, and are either collapsible or rigid. Some models are equipped with a one-way valve, while others have no valves. These devices are intended as lowcost, portable alternatives to plastic VHCs and are primarily designed for single-use, short-term applications. In contrast, reusable VHCs are typically constructed from durable plastic, feature dual one-way valves and are intended for long-term use with appropriate cleaning and maintenance.

Although some disposable spacers may resemble VHCs in terms of internal volume, they differ significantly in terms of materials, valve configuration and intended duration of use. These differences are crucial to consider when evaluating drug delivery efficiency and clinical relevance.

There is a scarcity of published research on the efficacy of commercially available disposable spacers.[6–11] In vivo studies have shown no significant difference in asthma symptom scores or peak flow when comparing nebulisers with the disposable paperboard spacer LiteAire (LA) (Thayer Medical, Tucson, Arizona, USA) for acute asthma treatment in adults.[6] However, comparisons between disposable and other types of spacers remain limited, especially in children. Additionally, financial conflicts of interest and the limitations of in vitro studies—where breathing parameters often do not accurately reflect real paediatric conditions—further complicate the evaluation process.[7 9 10] Our previous studies have demonstrated that data from one spacer cannot be extrapolated to another, even if they share similar properties such as material, shape and volume.[12 13] Although spacers are tested to meet regulatory requirements for safety, efficacy and quality prior to market approval, the rigour and clinical relevance of these tests remain unclear. This uncertainty reinforces the need for independent, rigorous testing of commercially available disposable spacers under clinically relevant, age-appropriate paediatric conditions.

International standards recommend assessing in vitro drug delivery of inhaled medications using cascade impactors. These devices measure the aerodynamic particle size distribution (APSD) of drug particles emitted from an aerosol source, determining their likelihood of reaching therapeutically significant regions of the respiratory tract. Particle size is critical, as optimal lung deposition occurs within the respirable range of 1–5 µm. For children, an even narrower range of 1–3 µm has been proposed as ideal.[14 15]

In this study, we aimed to evaluate the APSD of salbutamol, focusing on fine particle dose (FPD) and throat deposition, with three reusable VHCs, one disposable VHC and one disposable valveless spacer under normal and obstructive paediatric breathing patterns.

MATERIALS AND METHODS

Following international standards for in vitro inhaled drug testing, we used a Next Generation Impactor (NGI, Copley Scientific, Nottingham, UK) equipped with a mixing inlet and a child throat model (Child Alberta Idealized Throat, Copley Scientific, Nottingham, UK) (online supplemental figure S1). We used a child throat model that represents the anatomy of children aged 6–14 years, as there is currently no validated model available for younger children. A Breathing Simulator BRS 3100 (Copley Scientific, Nottingham, UK) was used to generate a sinusoidal wave pattern.

The spacers were connected to the throat model using a silicone adapter without a facemask and the system was tested for leaks before each run. The disposable spacers studied were LA and DispozABLE (Diz). The reusable VHCs examined were AeroChamber Plus Flow-Vu with mouthpiece, EasyChamber (EC) and OptiChamber Diamond. From the age of 4 years, children are generally able to use VHCs without a mask,[4 16] thus masks were excluded from this study.

Three sinusoidal breathing profiles were studied: two representing calm breathing and one representing obstructive breathing. The calm breathing profiles included profiles typical for a 4 years old: respiratory rate (RR) 24/min, tidal volume (V_t) 150 mL, inspiratory/expiratory (I/E) ratio 1 s/1.5 s and a typical 6 years old (RR 24/min, V_t 220 mL and I/E ratio 1 s/1.5 s). The obstructive breathing profile was characterised by RR 50/min, V_t 50 mL and an I/E ratio of 0.5 s/0.7 s. The parameters for calm breathing were estimated based on the expected heights of 4-year-old and 6-year-old children according to Finnish growth curves.[17] These heights were used to calculate RR, V_t, and I/E, and we then verified that the RR and I/E results aligned with recent reference values.[18]

Salbutamol delivery was generated using a pMDI (Ventoline Evohaler 100 µg/dose, GlaxoSmithKline, Evreux, France). A single dose (100 µg) was actuated into the test system after shaking the pMDI.[19 20] Following actuation, the breathing simulator was manually timed to perform five sinusoidal breathing cycles to draw the dose from the spacer. In vivo, a few breathing cycles are typically required for aerosol inhalation from spacers.[21] After completing five breathing cycles, samples were collected from the throat model and the eight NGI cups.

For each reusable VHC, one unit from three different manufacturing lots was tested, with each breathing pattern test repeated four times per VHC. The reusable VHCs were cleaned and dried after each test, in accordance with the manufacturer's instructions. For the disposable spacers, three new spacers were used for each test run, with each breathing pattern test repeated four times per spacer.

The test system preparation involved coating the NGI stage cups with a fixation solution to minimise particle bounce-off. Samples were collected by adding a solvent to the throat model and NGI cups. For each NGI part one vial was sampled and analysed by high-performance liquid chromatography carried out by Emmace Consulting AB (Lund, Sweden) with the following setup: mobile phase; Methanol/50 mM phosphate buffer pH 3.0 20/80 (vol/vol), pump flow rate; 1 mL/min, injection volume; 10 µL, detection wavelength; 224 nm, column; Symmetry (Waters), C18, 5 µm, 50 mm × 3.9 mm (ID). The method is linear between 0.1 and 31 µg/mL. The limit of quantitation is 0.2 µg/mL. The NGI stage cut-off diameters were determined based on the flow rate used, with interpolation between two adjacent stages.

Statistical analysis was performed using IBM SPSS Statistics for Windows, V.29. Since the data were not normally distributed, to assess the differences in delivered dose of salbutamol among spacers, the Kruskal-Wallis test was used. To minimise the risk of type 1 error associated with multiple comparisons and to maintain the overall familywise error rate below 0.05, the Bonferroni correction was applied with the adjusted significance level of $p<0.0083$.

RESULTS

The overall APSD and delivered doses at throat model and different stages of the impactor are given in figure 1, while FPD and throat deposition are presented in more detail in (figures 2–4). The APSD profile was similar in shape across the spacers in all breathing patterns with the highest dose peaking in the desired FPD range of 1–5 µm, but there seemed to be differences in FPD between breathing patterns and spacers (figure 1).

The median FPD level was significantly higher with all spacers in the calm breathing profiles (6-year-old and 4-year-old children) compared with obstructive breathing ($p<0.001$). Additionally, for EC and OptiChamber, there was a significant difference in median delivered FPD between the two calm breathing profiles, with a significantly higher dose in the 6-year-old breathing profile ($p<0.01$). The valved LA and the reusable AeroChamber had similar profiles and delivered doses.

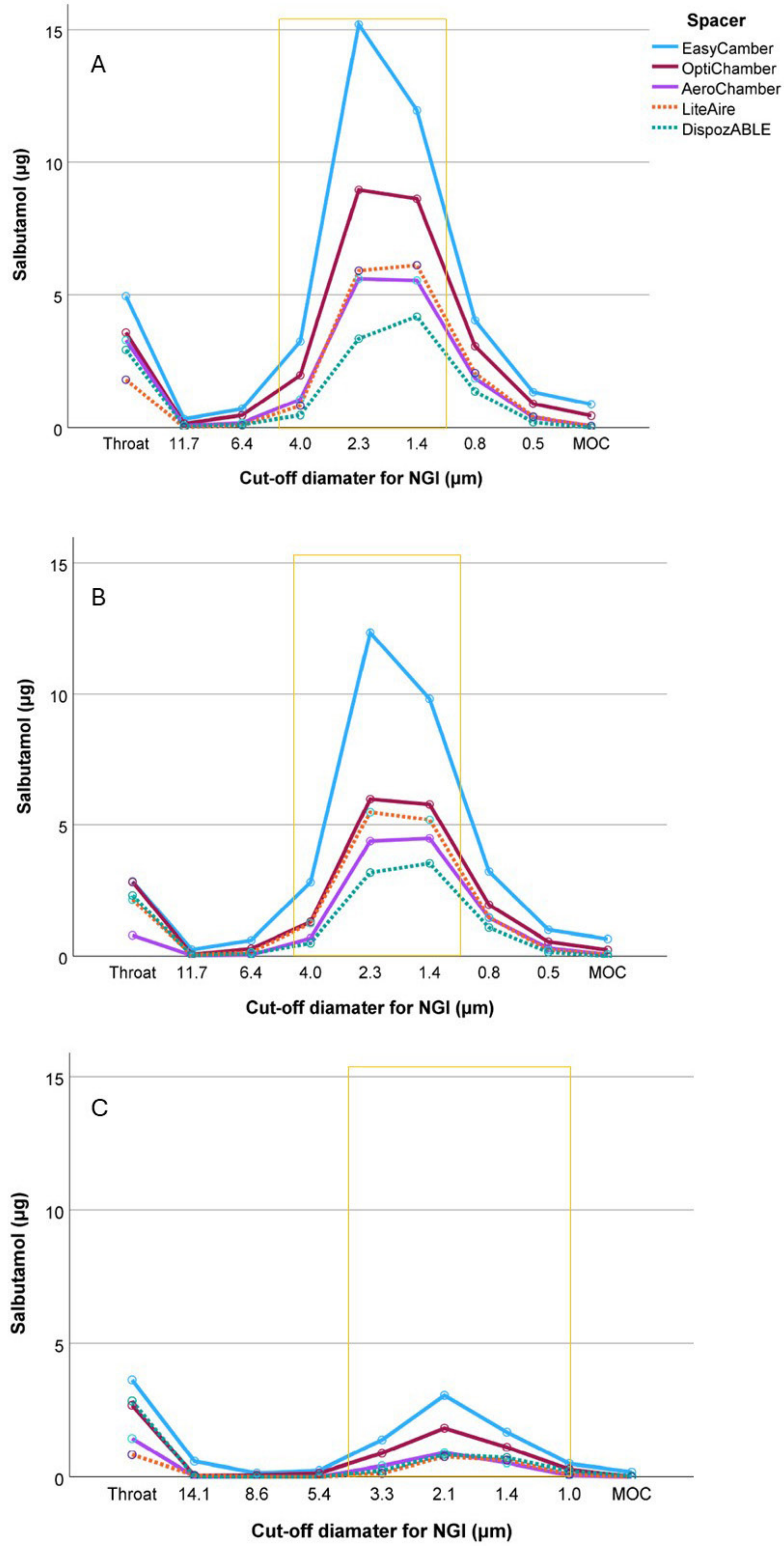

Figure 1 The amount of salbutamol in the throat model and in the different stages of the Next Generation Impactor (NGI) with three different breathing profiles and five different spacers. (A) Tidal breathing of a 6 years old (V_t 220 mL, RR 24 /min and I/E 1.0 s/1.5 s). (B) Tidal breathing of a 4 years old (V_t 150 mL, RR 24 /min and I/E 1.0 s/1.5 s). (C) Obstructive breathing (V_t 50 mL, RR 50 /min and I/E 0.5 s/0.7 s). Label claim: 100 µg/dose salbutamol (Ventoline Evohaler). Solid line indicates reusable spacer and dashed line indicates disposable spacer. The box represents the particle distribution within the 1–5 µm respirable range. I/E, inspiration/expiration; MOC, micro-orifice collector; RR, respiratory rate; Vt, tidal volume.

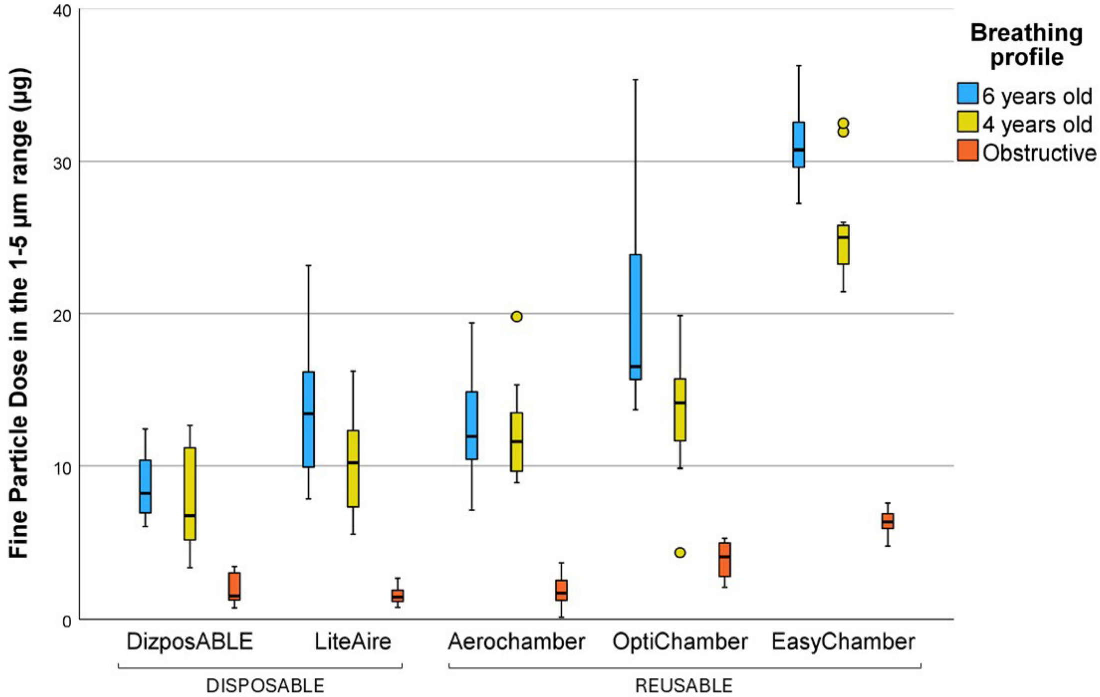

Figure 2 Fine particle dose in the respirable range 1–5 µm of 1 dose of salbutamol 100 µg/dose with three different breathing profiles and five different spacers. Tidal breathing of a 6 years old (V_t 220 mL, RR 24/min and I/E 1.0 s/1.5 s). Tidal breathing of a 4 years old (V_t 150 mL, RR 24/min and I/E 1.0 s/1.5 s). Obstructive breathing (V_t 50 mL, RR 50/min and I/E 0.5 s/0.7 s). Error bars: 95% CI. I/E, inspiration/expiration; RR, respiratory rate; V_t, tidal volume.

The median delivered FPD in the respirable range of 1–5 µm was significantly higher for EasyChamber compared with LA, Diz and AeroChamber in all the breathing profiles (figure 2 and table 1). EC also showed superior 1–5 µm particle delivery compared with OptiChamber in the 4-year-old profile. The disposable valveless Diz delivered the lowest amount of

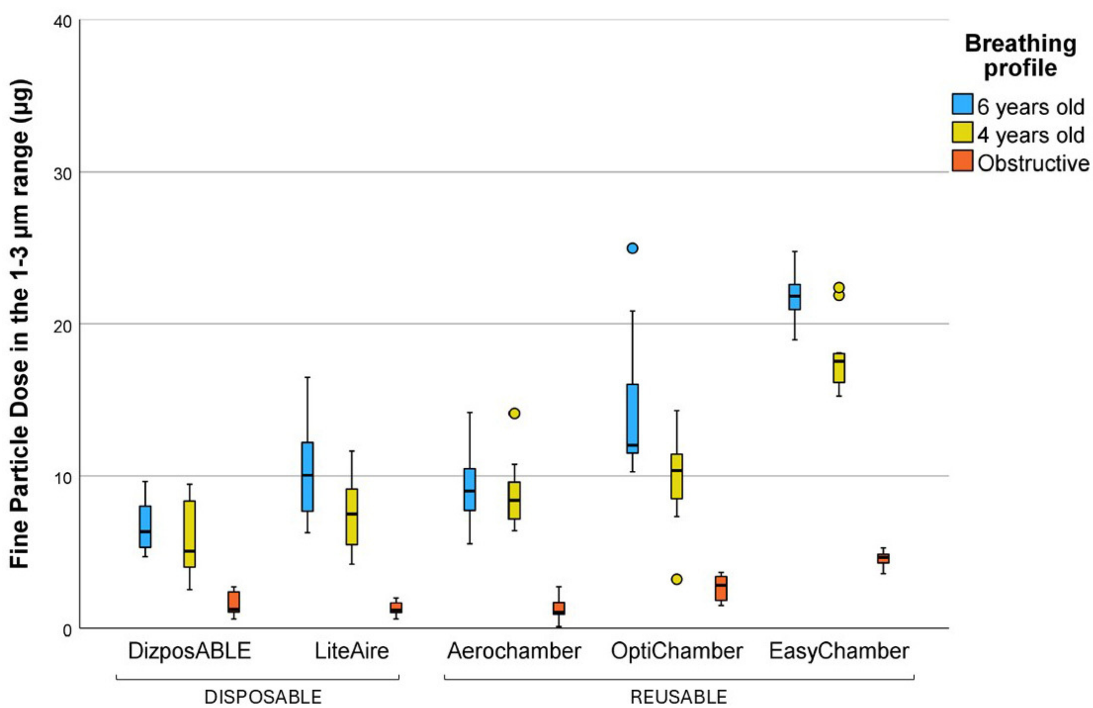

Figure 3 Fine particle dose in the respirable range 1–3 µm of 1 dose of salbutamol 100 µg/dose with three different breathing profiles and five different spacers. Tidal breathing of a 6 years old (V_t 220 mL, RR 24/min and I/E 1.0 s/1.5 s). Tidal breathing of a 4 year old (V_t 150 mL, RR 24/min and I/E 1.0 s/1.5 s). Obstructive breathing (V_t 50 mL, RR 50/min and I/E 0.5 s/0.7 s). Error bars: 95% CI. I/E, inspiration/expiration; RR, respiratory rate; V_t, tidal volume.

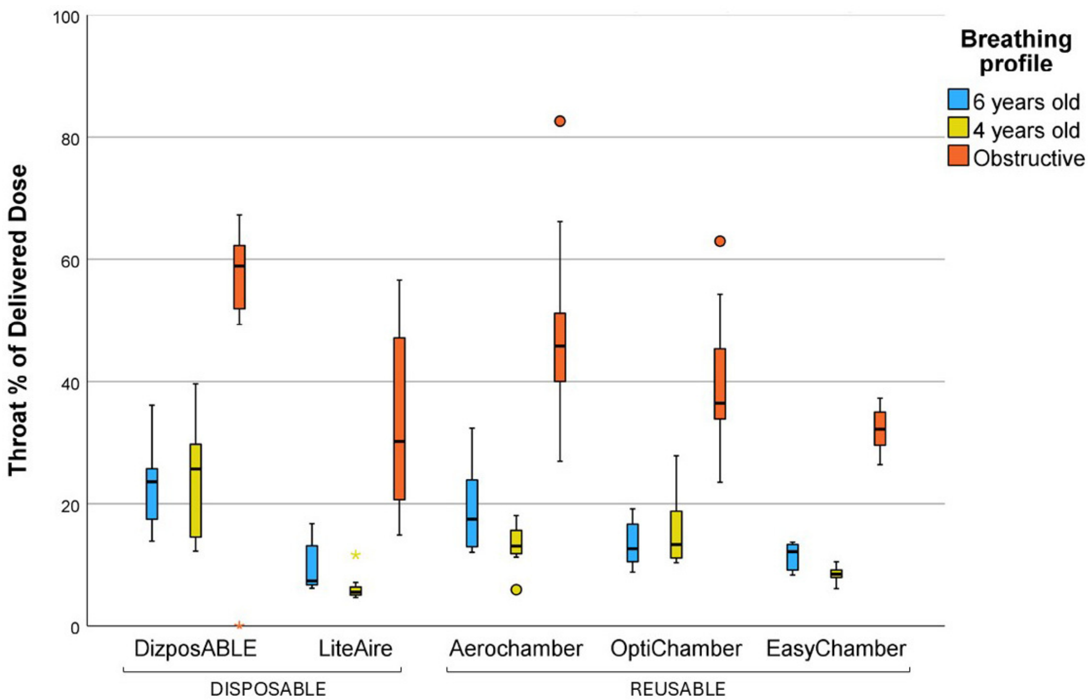

Figure 4 Throat deposition of salbutamol with three different breathing profiles and five different spacers. Tidal breathing of a 6 years old (V_t 220 mL, RR 24/min and I/E 1.0 s/1.5 s). Tidal breathing of a 4 years old (V_t 150 mL, RR 24/min and I/E 1.0 s/1.5 s). Obstructive breathing (V_t 50 mL, RR 50/min and I/E 0.5 s/0.7 s). Error bars: 95% CI. Label claim: 100 µg/dose salbutamol (Ventoline Evohaler). I/E, inspiration/expiration; RR, respiratory rate; V_t, tidal volume.

salbutamol during tidal breathing. During obstructive breathing the disposable LA and Diz as well as the reusable AeroChamber showed similarly low performance (figure 2 and table 1).

EC showed significantly higher median FPD also in the smaller particle range of 1–3 µm compared with any other spacer in the 4-year-old breathing profile and obstructive breathing (figure 3 and table 1). For the 6-year-old profile, the FPD 1–3 µm was significantly higher with EC compared with Diz, LA and AeroChamber. OptiChamber showed significantly higher FPD 1–3 µm delivery compared with Diz and AeroChamber in the 6-year-old breathing profile, as well as compared with LA during obstructive breathing (figure 3 and table 1).

The relative throat deposition was highest in obstructive breathing for all spacers (figure 3). Diz showed the highest relative throat deposition in all the breathing profiles and the difference was statistically significant compared with LA and EC in the calm breathing profiles and to LA, OptiChamber and EC in obstructive breathing. LA and EC showed the lowest relative throat deposition in the calm breathing profiles and EC in obstructive breathing.

DISCUSSION

This is the first publication to compare the APSD of salbutamol delivered via disposable paperboard spacers and reusable VHCs under various simulated paediatric breathing patterns that mimic real-life conditions in children under school age. Our study revealed significant differences between disposable and reusable spacers, as well as variations among spacers of the same type. The valveless Diz performed poorly overall. LA and AeroChamber exhibited remarkably similar FPD profiles and delivered dose in all setups despite notable differences in material and design. EC demonstrated superior performance compared with all other spacers in both the FPD 1–5 µm and FPD 1–3 µm ranges across all breathing patterns. The drug output of OptiChamber was higher than that of Diz, LA and AeroChamber in obstructive breathing and the calm breathing profile of a 6-year-old profile but not in the 4-year-old profile.

The performance of all spacers declined as V_t decreased. These results align with previous studies showing that a decrease in V_t reduces the delivered dose, particularly in cases of extremely low V_t during obstructive breathing.[12–14 22]

In our present study using salbutamol, there was no significant difference in the shape of the FPD profile between the spacers. However, in our previous in vitro study on the performance of pMDI+VHC with fluticasone propionate compared with EC, the FPD distribution of other VHCs (OptiChamber, AeroChamber and Babyhaler) was notably different, skewing towards particles below 2 µm.[12] These findings highlight that results from one molecule cannot be directly extrapolated to another when using the same spacer, due to differences in molecular behaviour.

Most studies report FPD in the 1–5 µm range. However, spacer performance may vary even between the 1–3 µm and 1–5 µm particle size ranges. In the 1–3 µm FPD range, we found more statistically significant differences favouring EC and OptiChamber compared with the 1–5 µm FPD range. The clinical significance of this finding remains uncertain, but it highlights the variability in spacer performance. As no regulatory acceptance criteria for FPD currently exist, such comparisons across different particle size fractions provide valuable context for interpreting device performance.

The performance of OptiChamber exhibited the greatest variability, while EC showed the least. In less controlled situations, such as in vivo conditions, the predictability and reproducibility of drug output and throat deposition may be even lower. This would further highlight the advantage of devices with more consistent performance.

The overall performance of a traditional VHC, EC, is indisputably superior to that of disposable spacers. Whenever possible,

Table 1 Pairwise comparison of FPD for 1–5 µm and 1–3 µm across spacers and the numerical values of median FPD 1–5 µm, FPD 1–3 µm and throat deposition

Breathing profile	Pairs*	Median FPD 1–5 µm (µg)	Median FPD 1–3 µm (µg)	Median throat deposition per cent of total delivered dose	1–5 µm Adj. Sig†	1–3 µm Adj. Sig†
6-year-old profile V_t 220 mL, I/E 1 s/1.5 s	**EC**–Diz	30.7–8.2	21.8–6.4	12.2–23.5	<0.001	<0.001
	EC–LA	30.7–13.5	21.8–10.0	12.2–7.3	0.001	<0.001
	EC–AC	30.7–11.9	21.8–9.0	12.2–17.5	<0.001	<0.001
	EC–OC	30.7–16.3	21.8–12.0	12.2–12.6	0.706	0.064
	OC–Diz	16.3–8.2	12.0–6.4	12.6–23.5	<0.001	<0.001
	OC–LA	16.3–13.5	12.0–10.0	12.6–7.3	0.489	0.221
	OC–AC	16.3–11.9	12.0–9.0	12.6–17.5	0.268	0.018
	AC–Diz	11.9–8.2	9.0–6.4	17.5–23.5	0.527	0.143
	AC–LA	11.9–13.5	9.0–10.0	17.5–7.3	1.000	1.000
	LA–Diz	13.5–8.2	10.0–6.4	7.3–23.5	0.288	0.143
4-year-old profile V_t 150 mL, I/E 1 s/1.5 s	**EC**–Diz	25.0–6.8	17.5–5.1	8.5–25.6	<0.001	<0.001
	EC–LA	25.0–10.2	17.5–7.5	8.5–5.5	<0.001	<0.001
	EC–AC	25.0–11.6	17.5–8.4	8.5–13.1	0.002	<0.001
	EC–OC	25.0–14.1	17.5–10.4	8.5–13.3	0.043	<0.001
	OC–Diz	14.1–6.8	10.4–5.1	13.3–25.6	0.040	0.143
	OC–LA	14.1–10.2	10.4–7.5	13.3–5.5	0.929	0.589
	OC–AC	14.1–11.6	10.4–8.4	13.3–13.1	1.000	0.143
	AC–Diz	11.6–6.8	8.4–5.1	13.1–25.6	0.433	1.000
	AC–LA	11.6–10.2	8.4–7.5	13.1–5.5	1.000	1.000
	LA–Diz	10.2–6.8	7.5–5.1	5.5–25.6	1.000	1.000
Obstructive V_t 50 mL, I/E 0.5 s/0.7 s	**EC**–Diz	6.4–1.5	4.7–1.2	32.2–58.9	<0.001	<0.001
	EC–LA	6.4–1.4	4.7–1.2	32.2–30.2	<0.001	<0.001
	EC–AC	6.4–1.7	4.7–1.0	32.2–45.8	<0.001	<0.001
	EC–OC	6.4–4.0	4.7–2.8	32.2–36.5	0.572	0.011
	OC–Diz	4.0–1.5	2.8–1.2	36.5–58.9	0.067	1.000
	OC–LA	4.0–1.4	2.8–1.2	36.5–30.2	0.009	0.143
	OC–AC	4.0–1.7	2.8–1.0	36.5–45.8	0.057	0.064
	AC–Diz	1.7–1.5	1.0–1.2	45.8–58.9	1.000	1.000
	AC–LA	1.7–1.4	1.0–1.2	45.8–30.2	1.000	1.000
	LA–Diz	1.4–1.5	1.2–1.2	30.2–58.9	1.000	1.000

*Results favouring the respective spacer are shown in bold.
†Significance values have been adjusted by the Bonferroni correction for multiple tests.
AC. AeroChamber Plus Flow-Vu; Adj. Sig, adjusted significance; Diz. DispoZABLE; EC. EasyChamber; FPD. fine particle dose; I/E. inspiratory/expiratory; LA. LiteAire; OC. OptiChamber Diamond; V_t. tidal volume.

the most effective VHC should be selected. On some measures, LA matched or even exceeded the performance of AeroChamber, while in others, there was no significant difference between LA and OptiChamber. Among the two disposable spacers, LA performed slightly better than Diz during tidal breathing, with significantly lower throat deposition. This may be attributed to Diz lacking valves, whereas LA features two one-way valves, as well as notable differences in their shape and overall design.

Disposable spacers cost only about one-fourth to one-tenth of reusable spacers and require no cleaning. In settings such as emergency departments, ambulances, lung function testing and other situations where cleaning, maintenance and storage of reusable VHCs are not feasible or practical, LA could serve as a cheaper, more compact, readily usable alternative. However, it is important to note that during obstructive breathing, LA and Diz do not perform as well as EC or OptiChamber. In such cases, the salbutamol dose may need to be adjusted to ensure an adequate therapeutic response. Environmental considerations related to spacer use are also important and should account not only for the carbon footprint of manufacturing and transportation but also for the environmental impact of cleaning procedures and medical waste generation. In clinical settings such as emergency departments, ambulances and urgent care centres, reusable plastic VHCs may be impractical. As they are intended for single-patient use, they should not be reused for another individual, even after cleaning. Consequently, they must either be discarded after use or given to the patient, both of which increase per-use costs and present logistical challenges. Notably, one of the disposable spacers evaluated in our study (ie, LA) is primarily composed of cardboard, making it lightweight, mostly biodegradable and potentially recyclable. This distinguishes it from conventional plastic-based disposable devices and may substantially reduce its environmental footprint. Although the increased use of single-use medical devices raises legitimate sustainability concerns, the adoption of eco-friendly materials such as cardboard represents a meaningful advancement. Such design innovations may enhance both the feasibility and acceptability of disposable spacers in acute care contexts where the use of reusable devices is often not viable.

Our methods adhere to international standards for in vitro testing of inhaled medication. We simulated breathing parameters that closely approximate real-life conditions. Children exhibit variable V_t and RRs, which change with growth.[23 24] As children age, their RR decreases, with median breaths per minute as follows: <1 year: 37–44; 1–3 years: 25–38; 3–6 years: 22–26; and 6–12 years: 18–22.[25] Conversely, V_t increases with age, averaging approximately 7–10 mL/kg of ideal body weight during early childhood.[24]

Our findings are based on an in vitro model, which may not fully represent in vivo outcomes. However, the in vitro approach allowed for the efficient and standardised comparison of multiple spacers under paediatric breathing profiles. The high level of control in this model helps to minimise confounding factors frequently encountered in clinical studies, such as variable cooperation, inadequate lip seal and inconsistent inhalation technique. Although direct extrapolation of in vitro FPD data to in vivo therapeutic outcomes is not possible, previous studies with dry powder inhalers have demonstrated a strong correlation between FPD and lung bioavailability.[26] Furthermore, clinical evidence suggests that the systemic bioavailability of fluticasone propionate is influenced by the choice of VHC, supporting the clinical relevance of our findings.[27]

Additional limitations include the use of only two paediatric breathing patterns, which, while physiologically relevant, do not capture the full spectrum of variability across the paediatric age range. As the only validated paediatric throat model currently available anatomically represents children aged 6–14 years, its use in testing with a simulated 4-year-old breathing pattern may introduce some bias and limit the accuracy of extrapolation to younger age groups. Facemasks were excluded from this study, as children from the age of 4 years are generally able to use VHCs without a facemask.[16 28] However, this exclusion may affect the generalisability of the findings to real-life clinical settings, where facemask use may still be used. These aspects should be explored in future studies to better reflect real-world use. These findings are specific to salbutamol and should not be directly extrapolated to other drug classes such as ICS.

Global guidelines recommend the use of pMDIs and spacers over nebulisers in mild and moderate asthma attacks.[4 5] However, implementing these recommendations in practice remains challenging, despite strong evidence, particularly in paediatric populations. Our study suggests that, in terms of performance, EC and OptiChamber are preferable, though LA performs comparably to some reusable VHCs. VHCs are generally preferred over simple spacers without a one-way valve, as the latter are prone to aerosol dispersion caused by uncoordinated exhalation into the chamber.[29] Our study showed poorer performance of Diz and hence supports this finding, reinforcing that the use of valveless spacers is not justified.

The adoption of new medical devices and practices is often a gradual process, frequently met with resistance due to familiarity with existing methods, concerns about efficacy and the need for additional training. Generating robust, high-quality evidence on inhalation devices is essential to reliably guide recommendations for the most effective options for children. Furthermore, comprehensive education and training for healthcare professionals are critical to ensuring the proper use of these devices, ultimately leading to improved treatment outcomes and better adherence to guideline-based care.

Disposable spacers could help overcome some barriers to transitioning from nebulisers to spacers in ERs and ambulances, potentially enhancing the clinical response to salbutamol treatment in wheezing patients while also reducing healthcare costs. Although traditional VHCs—especially EC and OptiChamber—generally outperform disposable spacers, certain valved disposable devices, such as LA, may be viable in specific situations where cost and practicality are key considerations.

Social media Peter Csonka, LinkedIn @peter-csonka-b4393b8a

Contributors Conceptualisation, methodology and writing—review and editing: LO, LL, BK and PC. Software and validation: LO, LL and PC. Formal analysis, data curation, writing—original draft and visualisation: LO and PC. Investigation: LO, BK and PC. Resources and funding acquisition: LL and PC. Supervision and project administration: PC. PC is responsible for the overall content as the guarantor. AI technology was used solely for grammar and language refinement in this submission. No AI was used for data analysis, content generation or research interpretation. The purpose of AI involvement was to ensure clarity and grammatical accuracy while maintaining the original meaning and integrity of the work.

Funding This work was supported by: Research Foundation for Pulmonary Diseases, The Finnish Medical Foundation, Tampere Tuberculosis Foundation, Jalmari and Rauha Ahokas Foundation and the Finnish Cultural Foundation: Pirkanmaa Foundation.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. This study does not involve patients; it is based on in vitro laboratory data. The study protocol, statistical analysis plan, collected data and data dictionary defining each field will be made available immediately following publication, contingent on the approval of a proposal and a signed data access agreement. All data requests should be submitted to the corresponding author for consideration.

ORCID iDs
Laura Ojanperä http://orcid.org/0009-0002-6429-7045
Lauri Lehtimäki http://orcid.org/0000-0003-1586-4998
Peter Csonka http://orcid.org/0000-0003-0819-7875

REFERENCES

1 Jurca M, Pescatore AM, Goutaki M, *et al*. Age-related changes in childhood wheezing characteristics: A whole population study. *Pediatr Pulmonol* 2017;52:1250–9.
2 Kuehni CE, Davis A, Brooke AM, *et al*. Are all wheezing disorders in very young (preschool) children increasing in prevalence? *The Lancet* 2001;357:1821–5.
3 Csonka P, Mertsola J, Klaukka T, *et al*. Corticosteroid therapy and need for hospital care in wheezing preschool children. *Eur J Clin Pharmacol* 2000;56:591–6.
4 Global Initiative for Asthma. Global strategy for asthma management and prevention. 2024. Available: https://ginasthma.org/
5 *British guideline on the management of asthma: a national clinical guideline*Revised edition. Edinburgh: Healthcare Improvement Scotland, 2019.
6 Dhuper S, Chandra A, Ahmed A, *et al*. Efficacy and cost comparisons of bronchodilatator administration between metered dose inhalers with disposable spacers and nebulizers for acute asthma treatment. *J Emerg Med* 2011;40:247–55.
7 Johnson JLH, Guthrie D, Hyde J, *et al*. The effect of a holding chamber on albuterol metered-dose inhaler product differences. *Ann Allergy Asthma Immunol* 2016;117:246–50.

8 Goodwin JL, Gerald LB, Johnson JLH, *et al*. Use of a disposable valved-holding chamber (spacer) in a school-based asthma trial. *J Allergy Clin Immunol Pract* 2018;6:307–9.
9 Sanders M, Bruin R. A Rationale for Going Back to the Future: Use of Disposable Spacers for Pressurised Metered Dose Inhalers. *Pulm Med* 2015;2015:176194.
10 Saeed H, Abdelrahim ME, Rabea H, *et al*. Evaluation of Disposable and Traditional Accessory Devices for Use With a Pressurized Metered-Dose Inhaler. *Respir Care* 2020;65:320–5.
11 Eynaud E, Leclerc L, Moreau-Neidhardt M, *et al*. Comparative performance study of paperboard disposable spacers versus commercial valved holding chambers for aerosol delivery. *Int J Pharm* 2024;666:124774.
12 Ojanperä L, Lehtimäki L, Huhtala H, *et al*. Inhaled corticosteroid delivery is markedly affected by breathing pattern and valved holding chamber model. *Pediatr Pulmonol* 2025;60:e27300.
13 Ojanperä L, Lehtimäki L, Kelemen B, *et al*. Salbutamol delivery in small children: Effect of valved holding chamber and breathing patterns. *J Allergy Clin Immunol Pract* 2024;12:509–11.
14 Amirav I, Newhouse MT, Minocchieri S, *et al*. Factors that affect the efficacy of inhaled corticosteroids for infants and young children. *J Allergy Clin Immunol* 2010;125:1206–11.
15 Cole CH. Special problems in aerosol delivery: neonatal and pediatric considerations. *Respir Care* 2000;45:646–51.
16 Csonka P, Tapiainen T, Mäkelä MJ, *et al*. Optimal administration of bronchodilators with valved holding chambers in preschool children: a review of literature. *Eur J Pediatr* 2021;180:3101–9.
17 Saari A, Sankilampi U, Hannila M-L, *et al*. New Finnish growth references for children and adolescents aged 0 to 20 years: Length/height-for-age, weight-for-length/height, and body mass index-for-age. *Ann Med* 2011;43:235–48.
18 Motamedi-Fakhr S, Iles R, Barker N, *et al*. Reference equations for tidal breathing parameters using structured light plethysmography. *ERJ Open Res* 2021;7:00050-2021.
19 Barry PW, O'Callaghan C. The effect of delay, multiple actuations and spacer static charge on the in vitro delivery of budesonide from the Nebuhaler. *Br J Clin Pharmacol* 1995;40:76–8.
20 Csonka P, Lehtimäki L. Antistatic treatment and salbutamol dosing have variable effect on drug delivery of valved holding chambers. *Pulm Pharmacol Ther* 2019;59:101857.
21 Schultz A, Le Souëf TJ, Venter A, *et al*. Aerosol inhalation from spacers and valved holding chambers requires few tidal breaths for children. *Pediatrics* 2010;126:e1493–8.
22 Csonka P, Lehtimäki L. Valved holding chamber drug delivery is dependent on breathing pattern and device design. *ERJ Open Res* 2019;5:00158-2018.
23 Nikander K, Denyer J. Breathing patterns. *Eur Respir Rev* 2000;10:576–9.
24 Rubin BK, Fink JB. Optimizing aerosol delivery by pressurized metered-dose inhalers. *Respir Care* 2005;50:1191–200.
25 Fleming S, Thompson M, Stevens R, *et al*. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. *The Lancet* 2011;377:1011–8.
26 Richardson CH, de Matas M, Hosker H, *et al*. Determination of the relative bioavailability of salbutamol to the lungs following inhalation from dry powder inhaler formulations containing drug substance manufactured by supercritical fluids and micronization. *Pharm Res* 2007;24:2008–17.
27 Blake K, Mehta R, Spencer T, *et al*. Bioavailability of inhaled fluticasone propionate via chambers/masks in young children. *Eur Respir J* 2012;39:97–103.
28 Bateman ED, Hurd SS, Barnes PJ, *et al*. Global strategy for asthma management and prevention: GINA executive summary. *Eur Respir J* 2008;31:143–78.
29 Lavorini F, Barreto C, van Boven JFM, *et al*. Spacers and Valved Holding Chambers-The Risk of Switching to Different Chambers. *J Allergy Clin Immunol Pract* 2020;8:1569–73.