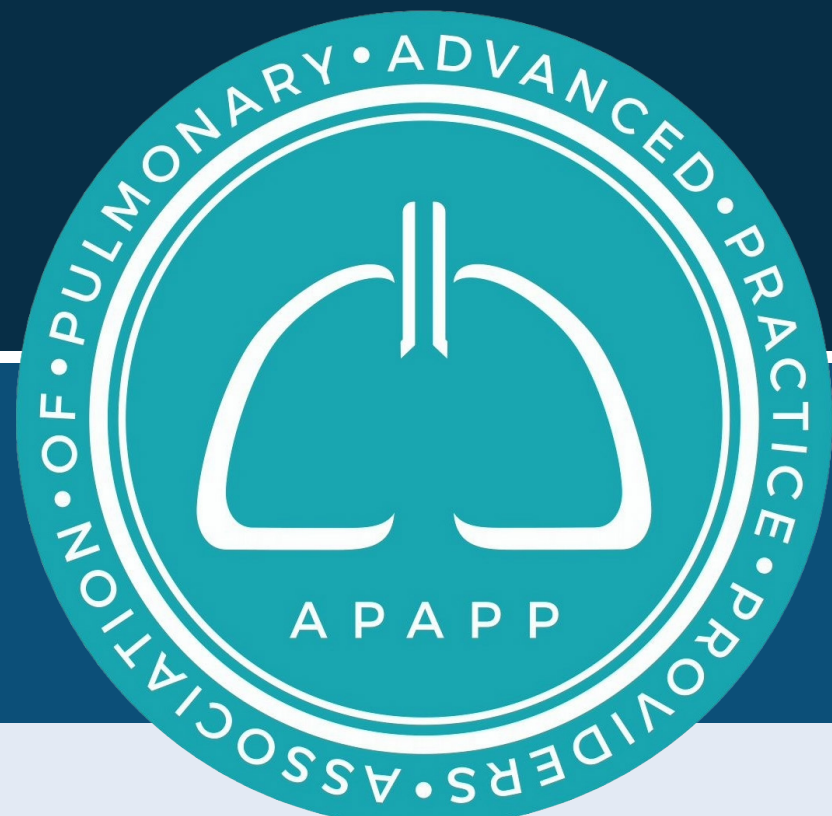


CAN PHARMACEUTICAL AUTO-SUBSTITUTIONS AFFECT OUTCOMES, AND DISEASE MANAGEMENT?

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BACKGROUND

Pharmaceutical auto-substitution may replace a prescribed valved holding chamber/spacer (VHC) with an alternative device assumed to be functionally equivalent. However, aerosol delivery depends on device-specific characteristics, including chamber geometry, volume, material, valve performance, and mask interface. Variability in these factors may alter the amount of drug available for inhalation.

This analysis evaluated whether differences among commercially available VHCs produce clinically relevant variation in inhaled corticosteroid dose, with implications for disease control.

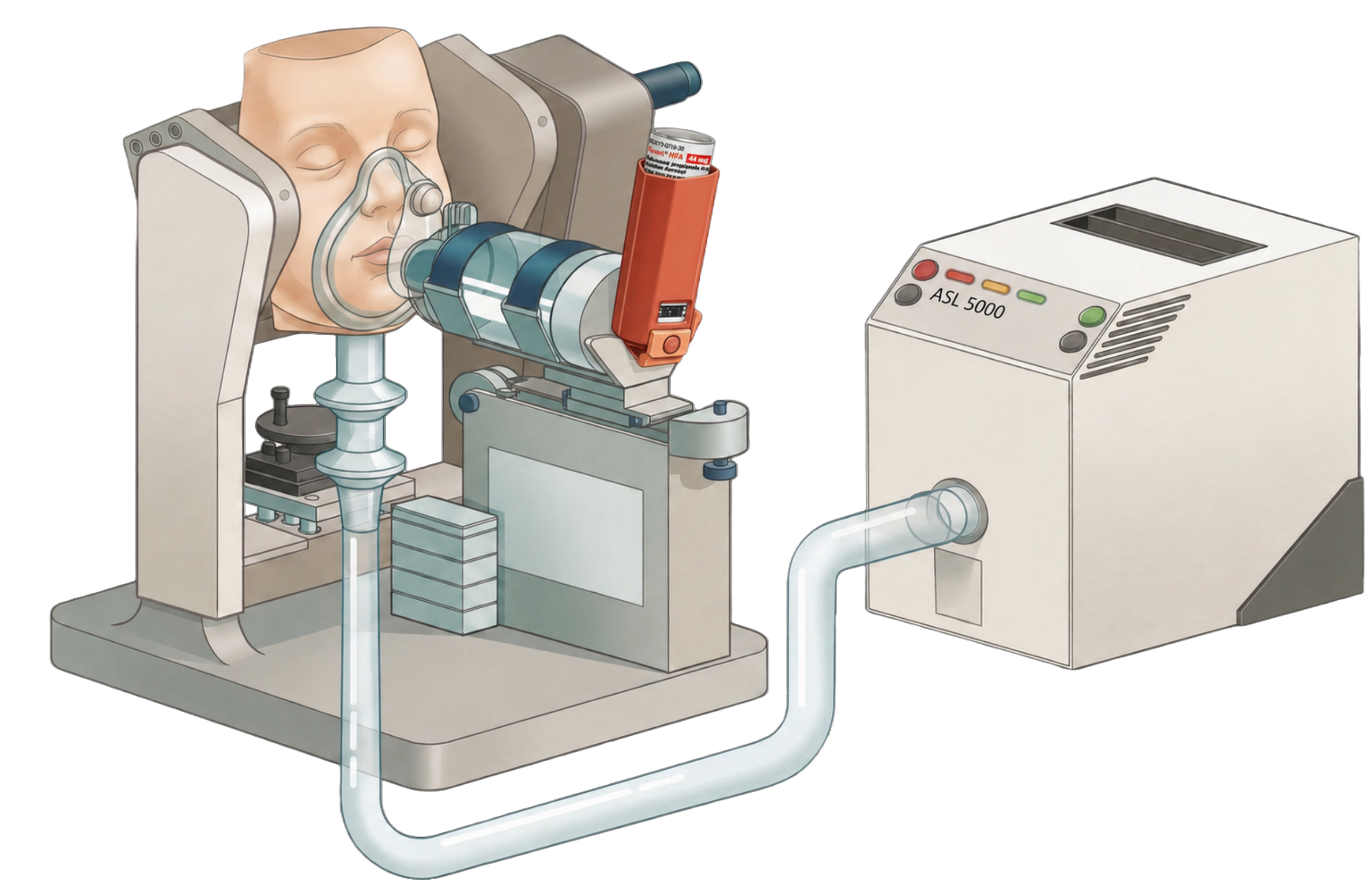
TESTING METHODS

Five VHCs with facemasks (n=5/group) were evaluated using an anatomically realistic oro-nasopharyngeal model (ADAM III) of a 4-year-old child.

Devices (AeroChamber Plus® Flow-Vu®, OptiChamber Diamond†, Compact Space Chamber Plus†, Vortex† and InspiraChamber†) were coupled to a breathing simulator (ASL 5000) via a distal filter to capture drug reaching the carina. The simulator included a 2-second coordination delay followed by tidal breathing (tidal volume 155 mL, I:E 1:2, rate 25 breaths/min).

Five actuations of fluticasone propionate MDI (44 µg) were delivered at 30-second intervals. Drug deposition within the chamber, facemask, and filter were quantified by HPLC. Carina deposition was used as a surrogate for lung-available dose.

ORO-NASOPHARYNGEAL MODEL (ADAM III) + ASL 5000

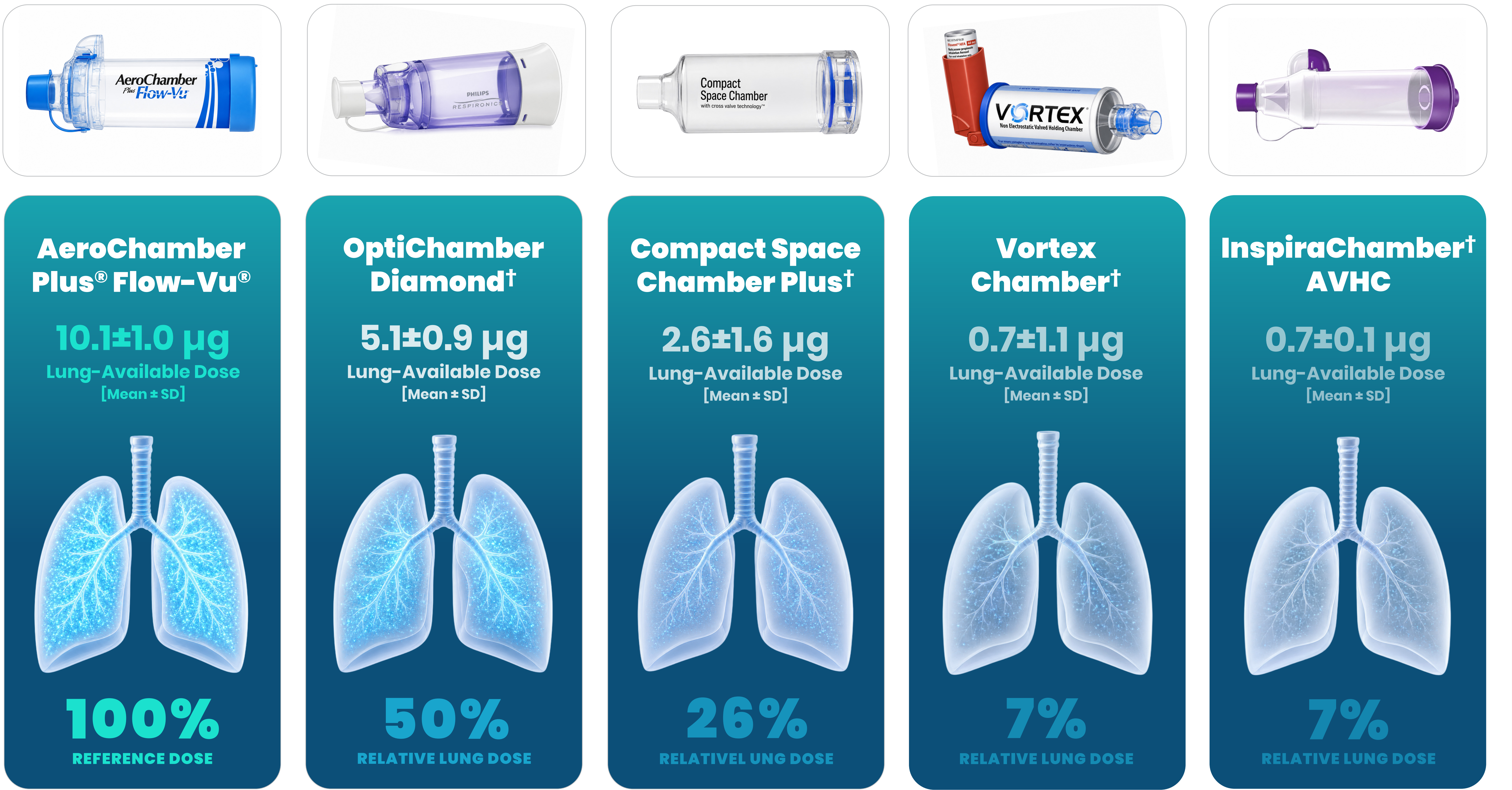


RESULTS

Marked variability in drug delivery was observed. Facemask and upper airway deposition were low but variable. Overall, a >10-fold difference in lung-available dose was observed between the different chambers.

DRUG DEPOSITION	AEROCHAMBER PLUS® FLOW-VU®	OPTICHAMBER DIAMOND† VHC	COMPACT SPACE CHAMBER PLUS†	VORTEX CHAMBER†	INSPIRACHAMBER† AVHC
Chamber	17.5 ± 1.6 µg	22.7 ± 2.7 µg	28.4 ± 3.3 µg	36.2 ± 3.8 µg	39.2 ± 2.7 µg
Facemask	1.4 ± 0.2 µg	3.6 ± 0.8 µg	0.1 ± 0.1 µg	0.5 ± 0.7 µg	1.0 ± 0.2 µg
Lung Dose	10.1±1.0 µg	5.1±0.9 µg	2.6±1.6 µg	0.7±1.1 µg	0.7±0.1 µg

NOT ALL VHCS DELIVER THE SAME LUNG-AVAILABLE DOSE. SAME MEDICATION. DIFFERENT RESULTS.



CONCLUSIONS

VHCs are not interchangeable in aerosol drug delivery.

Auto-substitution may alter the inhaled corticosteroid dose available to the patient. Reduced per-actuation delivery could plausibly contribute to suboptimal disease control and increased reliance on rescue medication. Device-specific performance should be considered in substitution practices.

