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Mitigating Fugitive Aerosols during Aerosol Delivery via High-Flow Nasal Cannula Devices

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Competing interests

Dr. Li declares to receive research funding from Fisher & Paykel Healthcare Ltd, Aerogen LLC, and Rice Foundation, lecture honorarium from American Associate for Respiratory Care, Aerogen LLC, Heyer Ltd, and Fisher & Paykel Healthcare Ltd. Dr. Li is also the section editor for Respiratory Care journal. Dr. Fink is Chief Science Officer for Aerogen Pharma Corp. Dr. Dhand reports remuneration from GSK Pharmaceuticals, Boehringer-Ingelheim, Mylan, Teva,

and Astra-Zeneca Pharmaceuticals outside the submitted work. Other authors have no conflicts to disclose.

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Authors' contributions

JL conceived and designed the study, implemented the study, analyzed the data, and revised the manuscript. AA implemented the study, interpreted the data, drafted and revised the manuscript. LH implemented the study and revised the manuscript. JBF conceived the concept, interpreted the data and revised the manuscript. RD interpreted the data and revised the manuscript. All authors reviewed and approved the final version.

Abstract

Background: Aerosol delivery via high-flow nasal cannula (HFNC) has attracted clinical interests in recent years. However, both HFNC and nebulization are categorized as aerosol generating procedures (AGPs). In-vitro studies raised concerns that AGPs had high transmission risk. Very few in-vivo studies examined fugitive aerosols with HFNC and nebulization via HFNC, and effective methods to mitigate aerosol dispersion are unknown.

Method: Two HFNC devices (Airvo2 and Vapotherm) with or without a vibrating mesh nebulizer (VMN) were compared; HFNC alone, surgical mask over HFNC interface, and HFNC with face tent scavenger were used in a random order for nine healthy volunteers. Fugitive aerosol concentrations at sizes of 0.3-10 μm were continuously measured by particle sizers placed at one and three feet from participants. On a different day, six of the nine participants received six additional nebulizer treatments via VMN or small volume nebulizer (SVN) with mouthpiece with/without an expiratory filter or facemask. In-vitro simulation was employed to quantify inhaled dose with VMN via Airvo2 and Vapotherm.

Results: Compared to baseline, neither HFNC device generated higher aerosol concentrations. Compared to HFNC alone, VMN via Airvo2 generated higher 0.3-1.0 μm particles (all $p<.05$) but VMN via Vapotherm did not. Concentrations of 1.0-3.0 μm particles with VMN via Airvo2 were similar with VMN and a mouthpiece/facemask but lower than SVN with a mouthpiece/facemask (all $p<.05$). Placing a surgical mask over HFNC during nebulization reduced 0.5-1.0 μm particles (all $p<.05$) to levels similar to the use of a nebulizer with mouthpiece and expiratory filter. In-vitro the inhaled dose with VMN via Airvo2 was ≥ 6 times higher than VMN via Vapotherm.

Conclusion: During aerosol delivery via HFNC, Airvo2 generated higher inhaled dose and consequently higher fugitive aerosols than Vapotherm. Simple measures, such as placing a surgical mask over nasal cannula during nebulization via HFNC, could effectively reduce fugitive aerosol concentrations.

Key words: High-flow nasal cannula; Nebulization; Aerosol generation procedure; COVID-19; Mitigation.

Introduction

High-flow nasal cannula (HFNC) devices deliver warmed and humidified oxygen at flows that exceed the subject's inspiratory flow with a fraction of inspired oxygen (F_IO_2) up to 1.0.[1] Use of HFNC reduces the need for intubation among hypoxemic patients. [1-4] In-line placement of a nebulizer with HFNC has been employed to deliver aerosolized medications,[5] such as inhaled epoprostenol for patients with pulmonary hypertension or refractory hypoxemia,[6,7] or inhaled albuterol for patients with asthma[8] or chronic obstructive diseases. [9,10] HFNC has been shown to be advantageous for nebulized therapy, compared to conventional aerosol delivery methods including nebulizers with facemask/mouthpiece, pressurized metered-dose inhalers (pMDIs), or dry powder inhalers (DPIs).[11] The nasal interface is more tolerable than a facemask or mouthpiece because it does not interfere with talking, eating, and drinking. This is particularly important for subjects who require long-term inhalation of aerosolized medication, such as continuous albuterol administration for patients with asthma,[8] or inhaled epoprostenol for patients with pulmonary hypertension and/or refractory hypoxemia.[6,7]

Both HFNC and aerosol therapy are categorized as aerosol generating procedures (AGPs).[12-14] In particular, nebulization was found to increase aerosol concentration in the subject's vicinity [15] and exhaled air dispersion distance with nebulization was higher than that with a simple oxygen mask or noninvasive ventilation.[16] When trans-nasal aerosol delivery was implemented in-vitro, fugitive aerosols could still be detected at 2.2 meters from the manikin, and it was estimated that a person standing at 0.8 meter and 2.2 meters from the manikin would be exposed to 8.5% and 3.2% of the medication, respectively.[17] Concerns about the risks of aerosol transmission limited the utilization of AGPs, including HFNC and nebulization, increasing use of alternative modalities of treatment, such as ventilators or pMDIs, leading to reported shortage of these

resources in the COVID-19 pandemic.[18] However, there is lack of in-vivo evidence that fugitive aerosol generation during trans-nasal aerosol delivery could transmit infection.

Methods to minimize the risk of bioaerosol transmission, in order to protect health care workers and further prevent spread of SARS-CoV-2 virus are the subject of ongoing discussion.[19] Placing a surgical mask over HFNC was found to significantly reduce aerosol particle concentrations at a distance of 1 and 3 feet from subjects,[20] however its effects during trans-nasal aerosol delivery is unknown. In addition, a face tent scavenger (Vapotherm inc, Exeter, NH) that continuously suctions subject's exhaled aerosol particles has recently been introduced with little information on its ability to reduce fugitive aerosols.

Therefore, we aimed to seek the most effective modality to reduce the fugitive aerosol concentrations during trans-nasal aerosol delivery. Accordingly, we investigated the concentrations of fugitive aerosols generated by two commonly used HFNC devices (Airvo2 and Vapotherm) with and without the in-line placement of a nebulizer. We also explored the ability of a surgical mask or a face tent scavenger to mitigate fugitive aerosols generated during trans-nasal aerosol delivery with HFNC.

Methods

This study has both an in-vivo and an in-vitro component. The in-vivo study was conducted to evaluate fugitive aerosol concentrations when HFNC devices (Airvo2 versus Vapotherm) were employed alone or with in-line placement of a vibrating mesh nebulizer (VMN). In-vitro study was implemented to assess the inhaled dose of aerosol delivery via the two HFNC devices.

In-vivo study

A prospective randomized cross-over trial was registered at clinicaltrials.gov (NCT04681599) with approval of the Ethics Committee at Rush University (approval No. 20121804-IRB01). Healthy adults aged 18 to 65 years were included in the study. Exclusion criteria included subjects with chronic lung disease, upper airway anatomical abnormalities, uncontrolled diabetes, hypertension, or untreated thyroid disease; pregnancy; positive COVID-19 test or any COVID-19 related symptoms (including sore throat, cough, body aches or shortness of breath for unknown reasons, loss of taste or smell, and fever ≥ 100 °F) within 21 days.

After reading study recruitment advertisement that was posted in respiratory care department in Rush university medical center, nine healthy subjects volunteered to participate in the study and were consented. The study was implemented in an intensive care unit room that is 3.65×3.65×2.8 m^3 with air exchange frequency of 6 times/hour. Two aerosol particle sizers (Model 3889, Kanomax, Andover, NJ) were placed at 1 and 3 feet from subjects who were sitting on a chair, to continuously measure the fugitive aerosol concentrations at sizes of 0.3-10μm (Figure 1). Throughout the study session, the door of the room was closed and talking, eating or moving around were discouraged. The investigator wore an N95 mask and remained in the room with the participant. Participants wore N95 masks during baseline and 15-minute intervals between experiments to minimize aerosol generation.

Fugitive aerosol concentrations were compared between Airvo2 (Fisher & Paykel Healthcare Ltd, Auckland, New Zealand) and Vapotherm (Vapotherm Inc, Exeter, NH). HFNC device alone, a surgical mask over HFNC interface, and HFNC with a face tent scavenger were tested in a random order (Figure 2). The scavenger was connected to a vacuum pressure of -100 mmHg. The HFNC flow was set at the highest level that the participant could tolerate, with the temperature set at 37°C. The size of nasal prongs was chosen based on nostril size. During trans-

nasal aerosol delivery, a VMN (Aerogen Solo, Aerogen Ltd., Galway, Ireland) was placed at the humidifier, and 3mL of saline was used for each nebulization, which lasted 8-10 minutes, plus 15 minutes interval, thus each test took approximately 15 minutes. On a different day, six of the nine participants returned to receive six additional nebulizer treatments, a small volume nebulizer (SVN, AirLife 002446, CareFusion, Yorba Linda, CA) and a VMN were used with a mouthpiece, a mouthpiece with an expiratory filter and an aerosol facemask in a random order (Figure 2).

The mean aerosol concentration for each particle size was measured from the beginning to the end of each test. Since six additional tests were completed on different days, due to the variance of baseline aerosol concentrations in the room, the fugitive aerosol concentrations generated by each device were calculated in proportion to baseline aerosol concentrations on the same day. In addition, participants self-evaluated comfort on the device and interface after use, utilizing a five-point Likert scale scoring from 1 (very uncomfortable) to 5 (very comfortable).

In-vitro study evaluating trans-nasal aerosol delivery via Airvo2 versus Vapotherm

An in-vitro study was conducted to evaluate the effectiveness of aerosol delivery via Airvo2 and Vapotherm. A simulated adult manikin (Laerdal adult airway management trainer, Stavanger, Norway) with appropriate upper airway anatomy was utilized (Figure 3), with a collecting filter (Respirgard 303, CareFusion, San Diego, CA) attached between the distal end of the manikin's trachea and one chamber of a two-chamber model lung (TTL, Michigan Instruments, Grand Rapids, MI). The two chambers could be moved together, displacement of one chamber that was connected to a critical care ventilator (Drager XL, Drager, Lübeck, Germany) caused the other chamber to rise and generate negative pressure, thereby simulating spontaneous breathing.

A large size adult nasal cannula was placed on the manikin's nares and connected to an adult HFNC circuit.

For each HFNC device, different flows tested were 20, 40, 60 L/min for Airvo2, and 20 and 40 L/min for Vapotherm (unable to operate at 60 L/min). Albuterol (2.5mg in 3mL) was placed in the VMN for each run. After nebulization, the collecting filter was removed and eluted with 10 mL solution (0.1M HCl mixed with 20% ethanol) and analyzed with spectrophotometry at 276 nm. The inhaled dose was calculated by determining the amount of albuterol captured on the collecting filter as a percentage of the nominal dose (2.5mg).

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median (Inter-Quartile Range [IQR]) based on the distribution of variables, which was analyzed by Kolmogorov-Smirnov test. Paired t test or Wilcoxon test was used to compare the differences of fugitive aerosol particle concentrations or inhaled doses between two interfaces, depends on the normality of the data distribution. Subject comfort was compared by Wilcoxon test. $P<.05$ was statistically significant. Data analysis was conducted with SPSS software (SPSS 26.0 for Windows; SPSS; Chicago, IL).

Results

In-vivo comparisons of Airvo2 vs Vapotherm with different interfaces

Nine subjects (8 females) were enrolled in the study, aged at 27 (26, 31) years with height of 167.5 ± 5.3 cm. Airvo2 and Vapotherm were employed with highest tolerable flows at 50 (42.5, 50) L/min and 30 (22.5, 30) L/min, respectively.

There was no significant difference on the fugitive aerosol concentrations generated at all particle sizes between Airvo2 and Vapotherm (Figure 4. To simplify the report, the rest of the results only report the particle concentrations at 1 foot from participants. Compared to baseline, aerosol concentrations were no different with use of either HFNC device and were not influenced by placing a surgical mask over the nasal cannula or use of a face tent scavenger (Figure 5a and 5b). When VMN was placed in-line with Airvo2, fugitive aerosol concentrations were higher than Airvo2 alone at particle sizes of 0.3-1.0μm (all $p<.05$). (Figure 6) In contrast, no significant differences were found for Vapotherm with versus without VMN incorporation. Compared to VMN via Vapotherm, use of VMN via Airvo2 generated higher 0.3-1.0μm particles (all $p<.05$) (Figure 6). During trans-nasal aerosol delivery with Airvo2, aerosol concentrations at particle size of 1.0μm were significantly reduced when a surgical mask was placed over nasal cannula ($p=.028$) (Figure 7a). On the other hand, use of a face tent scavenger did not influence particle concentrations of any size. No significant differences in aerosol concentrations were found with versus without the use of a surgical mask or a face tent scavenger when VMN was placed in-line with Vapotherm (Figure 7b).

Participants reported similar levels of comfort with Airvo2 and Vapotherm with or without the use of a surgical mask or a scavenger, except use of Airvo2 with a scavenger had a lower comfort score than Airvo2 alone [3.0 (2.5, 4.0) vs 4.0 (3.0, 5.0), $p=.038$] (Figure 8).With VMN placed in-line with HFNC, comfort scores were lower than HFNC alone for both Airvo2 [3.0 (3.0, 4.0) vs 4.0 (3.0, 5.0), $p=.059$] and Vapotherm [3.0 [1.5, 4.5) vs 4.0 (3.5, 5.0), $p=.38$), largely attributed to condensation from the nasal cannula. With surgical mask over the nasal cannula, participants reported lower comfort scores for Vapotherm and VMN than Vapotherm alone (3.0 (1.5, 3.5) vs 4.0 (3.5, 5.0), $p=.028$] (Figure 8).

In-vivo comparisons of fugitive aerosol concentrations between trans-nasal aerosol delivery and nebulizer with a mouthpiece or a facemask

When comparing trans-nasal aerosol delivery to conventional nebulizers with mouthpiece/facemask, in-line placement of VMN with Airvo2 generated lower fugitive aerosol concentrations than VMN with a facemask for 1.0μm particles (p=.046), but the results were similar to those with a VMN and mouthpiece (Figure 9a). VMN via Airvo2 generated lower fugitive aerosol concentrations than SVN with a mouthpiece or a facemask at particles of 1.0-3.0μm (all p<.05) (Figure 9b). Placing an expiratory filter with mouthpiece reduced fugitive aerosol concentrations for both VMN and SVN, which were lower than VMN with Airvo2 for 5.0-10.0μm particles (all p<.05) but similar to the results when wearing a surgical mask over the nasal cannula.

In-vitro study evaluating the inhaled dose delivered by Airvo2 compared to Vapotherm

The inhaled dose of albuterol was an order of magnitude higher when delivered via Airvo2 than Vapotherm with HFNC flow of 20 L/min (12.9±0.9 vs 1.3±0.1%, p=.05) and > 6 times higher at 40 L/min (5.0±0.2 vs 0.8±0.1%, p=.05) (Table 1). The inhaled dose increased as HFNC flow decreased for both Airvo2 (p=.027) and Vapotherm (p=.024).

Discussion

In this study, we found that (1) neither HFNC device when used alone generated higher aerosol concentrations compared to baseline values; (2) fugitive aerosol concentrations were higher when a VMN was placed in-line with Airvo2, in contrast no differences in aerosol concentrations were observed when VMN was used with Vapotherm; (3) during trans-nasal aerosol delivery via Airvo2, fugitive aerosol concentrations were similar to VMN with a

mouthpiece but lower than VMN and facemask or SVN with mouthpiece/facemask; and (4) placing a surgical mask over nasal cannula reduced fugitive aerosol concentrations but a similar effect was not seen with use of a face tent scavenger. In the in-vitro study, we found a several-fold higher inhaled dose with VMN via Airvo2 than VMN via Vapotherm, regardless of HFNC flows.

Use of a HFNC alone did not generate higher fugitive aerosol concentrations with either Airvo2 or Vapotherm. This observation agreed with previous studies that assessed fugitive aerosol concentrations among healthy volunteers during HFNC therapy.[21,22] Similar to the study conducted by Takazono and coworkers, we did not find significant reduction in fugitive aerosol concentrations by wearing a surgical mask over nasal cannula during quiet breathing.[20] In COVID-19 patients, we previously reported that fugitive aerosol concentrations were reduced after wearing a surgical mask over HFNC.[20] This difference is probably due to the more frequent respiratory AGPs in subjects, such as talking, forced expirations or coughing, which generate higher fugitive aerosol concentrations compared to healthy volunteers.[23-25]

Placing VMN in-line with Airvo2 generated higher fugitive aerosol concentrations than VMN via Vapotherm. This might be explained by the results of our in-vitro study that found 6-10 times higher inhaled dose with VMN via Airvo2 than VMN via Vapotherm. Similarly, Perry and colleagues reported little to no inhaled dose delivered with Vapotherm when VMN was placed proximal to the nasal cannula.[26] The lower inhaled dose as well as fugitive aerosol concentrations with Vapotherm might be explained by the design and structure of the Vapotherm device, which generates high velocity gas through a distinctive coaxial design that runs humidified gas between inner and outer lumens of the circuit tubing. The high velocity gas, small size of the humidifier chamber and circuit lumens trap aerosol in the circuit, rather than emitting it through the nasal cannula. Thus, the Vapotherm design does not appear to be ideal for trans-nasal aerosol delivery.

In our previous study that assessed fugitive aerosol concentrations during nebulization with different interfaces, we found that the face tent scavenger significantly reduced fugitive aerosol concentrations when a facemask was utilized with both SVN and VMN.[27] However, when VMN was placed in-line with Airvo2 in the current study, we did not find differences of fugitive aerosol concentrations with and without the use of a face tent scavenger, whereas placing a surgical mask over the nasal cannula significantly mitigated fugitive aerosols. This difference might be explained by the anatomic structures of both interfaces and their method of sealing. The surgical mask firmly covers the nose and mouth area and can filter the aerosols leaked from the nasal cannula, while the face tent scavenger is manufactured with an open top which may allow aerosol particles to escape, even with the application of negative pressure to continuously suction the exhaled gas. The discrepancy in the effectiveness of the scavenger to reduce fugitive aerosol concentrations between nebulizer with a facemask and nebulizer with HFNC could be explained by the longer distance from the scavenger to the nasal cannula than to the nebulizer facemask.

Our results provide valuable clinical implications for administering aerosol via HFNC in an effective and safe manner. With the exception of our experience with Vapotherm, aerosol delivery via HFNC is an effective and safe route for aerosol delivery, with a lower risk of transmitting infection than a nebulizer with a facemask or a mouthpiece. Aerosol delivery via HFNC is less likely to be contaminated, since the nebulizer is placed at the humidifier that is further away from the subject.[28] In addition, we found that fugitive aerosol concentrations with VMN via Airvo2 was lower than VMN or SVN with a facemask and SVN with a mouthpiece.

Wearing a surgical mask can further reduce the fugitive aerosol concentrations during trans-nasal aerosol delivery, with levels that are similar to those with use of mouthpiece and exhalation filter. Wearing a surgical mask has additional practical advantages, especially for use

with a subject who is coughing. Subjects may cough at any time during nebulization, sometimes provoked by aerosolized medication, and it is not realistic to ask subjects to cough through the mouthpiece or to remove the mouthpiece and wear a surgical mask while coughing. Thus, using HFNC to deliver aerosolized medication and putting a surgical mask over the nasal cannula could be a practical method for aerosol delivery in critically ill patients with respiratory contagious diseases. Of course, clinicians should maintain a distance of 6 feet from patients, and wear appropriate PPE when providing aerosol therapy for patients. Lastly, the number of people inside the patient room should be minimized during aerosol therapy.

There are some limitations to our study. First, this study was conducted among healthy subjects that have different breathing patterns than the patients who suffer from respiratory diseases. Patients have more tendency to generate productive cough during trans-aerosol delivery which can substantially impact the findings. Thus, further clinical studies on patients with varying respiratory patterns is warranted to validate our findings. 0 Second, all the experiments were performed, and corresponding measurements were recorded in one ICU room at one hospital. Measurements may differ in other hospital rooms depending on the room conditions, such as air exchange frequency and room volme.[25] Thirdly, the fugitive aerosol concentrations were found to be slightly different with flow settings at 30 to 60 L/min during HFNC therapy,[21,24] and our in-vitro study found the aerosol deposition decreased as HFNC flow increased.[29] While we only investigated the maximum tolerable flow settings in this study, the effects of various HFNC flows on the fugitive aerosol concentrations during trans-nasal aerosol delivery need further investigation. Fourthly, we placed the particle counter at 1 foot behind and to the side of the participant, as for convenience to stabilize the particle counter, the aerosol concentrations especially the large particles might vary at different position, future studies with more particle

counter placements are needed. Lastly, our study used aerosol particle concentrations to indirectly evaluate the bioaerosol transmission risk, and we did not investigate the virus load nor its infectivity.[30]

Conclusion

HFNC alone did not generate higher fugitive aerosol concentrations than baseline for either Airvo2 or Vapotherm. Compared to HFNC alone, in-line placement of VMN via Airvo2 produced higher fugitive aerosol concentrations but VMN via Vapotherm did not, consistent with 6–10 times greater inhaled dose with Airvo2 vs Vapotherm measured in-vitro. The fugitive aerosol concentrations with VMN via Airvo2 were similar to VMN with a mouthpiece but lower than VMN or SVN with a facemask and SVN with a mouthpiece. Placing a surgical mask over nasal cannula during aerosol delivery via HFNC could effectively reduce fugitive aerosol concentrations.

Acknowledgement

We thank all the volunteers for generously sharing their time to participate in this lengthy study.

Quick Look

Current Knowledge

Aerosol delivery via high-flow nasal cannula (HFNC) has attracted clinical interests in recent years. Both HFNC and aerosol therapy have been considered as aerosol generating procedure (AGP) during COVID-19 pandemic. However, evidence is lacking about the fugitive aerosol concentrations generated during trans-nasal aerosol delivery and the effective method to reduce the fugitive aerosol concentrations.

What This Paper Contributes to Our Knowledge

High flow nasal cannula devices alone did not generate higher fugitive aerosol concentrations than baseline. Trans-nasal aerosol delivery via Airvo2 produced higher fugitive aerosol concentrations than trans-nasal delivery via Vapotherm, which can be explained by the low inhaled dose of aerosol delivered with Vapotherm in the in-vitro studies. Simple measures such as utilizing surgical mask on top of nasal prongs during trans-nasal aerosol delivery reduced fugitive aerosol particle concentrations.

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Figure legends

Figure 1. In-vivo study set up

The study participant sat in a chair to receive the nebulization via a VMN placed in the humidifier of Airvo2, a face tent scavenger connected with a vacuum pressure of -100 mmHg was placed surrounding his face. Two particle sizers were placed at 1 and 3 feet from the participant to continuously measure fugitive aerosol concentrations at 0.3-10 μm. The study investigator wore a N95 mask and stayed with the participant throughout the study.

VMN, vibrating mesh nebulizer.

Figure 2. Study flowchart

VMN, vibrating mesh nebulizer; SVN, small volume nebulizer.

Figure 3. In-vitro study set up

HFNC, high-flow nasal cannula; VMN, vibrating mesh nebulizer.

Figure 4. Fugitive aerosol concentrations with Airvo2 vs Vapotherm

X-axis presents different sizes of aerosol particles, Y-axis presents the concentrations of aerosol particles (/m^3).

Compared to baseline, HFNC did not generate higher fugitive aerosol concentrations for both Airvo2 and Vapotherm. No significant differences of fugitive aerosol concentrations between the two device at 1 foot from participants (Fig 4a), while at 3 feet away, Vapotherm had lower fugitive aerosol concentrations than Airvo2 at particle sizes of 1.0-3.0 μm (all $p<.05$) (Fig 4b).

Figure 5. Fugitive aerosol concentrations with mitigation devices for HFNC

Compared to the HFNC alone, wearing a surgical mask over the nasal cannula or wearing a face tent scavenger did not reduce fugitive aerosol concentrations for Airvo2 (Fig 5a) or Vapotherm (Fig 5b) at all particle sizes.

HFNC, high-flow nasal cannula

Figure 6. Fugitive aerosol concentrations of HFNC with versus without VMN.

X-axis presents different sizes of aerosol particles, Y-axis presents the concentrations of aerosol particles (/m^3).

Compared to HFNC alone, in-line placement of VMN via Airvo2 generated higher fugitive aerosol concentrations at particle sizes of 0.3-1.0 μm (all $p<.05$) but Vapotherm did not..

Fugitive aerosol concentrations were higher with VMN via Airvo2 than VMN via Vapotherm with particle sizes of 0.3-1.0 μm.

HFNC, high-flow nasal cannula; VMN, vibrating mesh nebulizer.

Figure 7. Fugitive aerosol concentrations of aerosol delivery via HFNC with different interfaces

X-axis presents different sizes of aerosol particles, Y-axis presents the concentrations of aerosol particles (/m^3).

When VMN was placed in-line with Airvo2, wearing a surgical mask over nasal cannula significantly reduced fugitive aerosol concentrations at particle sizes 1.0 μm (p=.028) (Fig 7a), while no differences in aerosol concentrations were observed with use of a face tent scavenger.

When VMN was placed in-line with Vapotherm, no significant differences of fugitive aerosol concentrations were found among different interfaces (Fig 7b).

VMN, vibrating mesh nebulizer;

Figure 8. Participant comfort score with different devices and interfaces

Participants reported similar levels of comfort with Airvo2 and Vapotherm with or without the use of a surgical mask or a scavenger, except use of Airvo2 with a scavenger had a lower comfort score than Airvo2 alone. When VMN was placed in-line with HFNC, the comfort scores were lower than HFNC alone, especially for Vapotherm. With the use of a surgical mask over the nasal cannula, participants reported lower comfort scores for Vapotherm and VMN than Vapotherm alone.

HFNC, high-flow nasal cannula; VMN, vibrating mesh nebulizer.

Figure 9. Fugitive aerosol concentrations of trans-nasal aerosol delivery versus a nebulizer with a mouthpiece or a facemask

X-axis presents different sizes of aerosol particles, Y-axis presents the times of fugitive aerosol particle concentrations to baseline.

Fugitive aerosols generated during the in-line placement of VMN via Airvo2 were similar to VMN with a mouthpiece or a facemask (Figure 9a), but lower than SVN with a mouthpiece or a facemask at particles of 1.0-3.0 μm (all $p < 0.05$) (Figure 9b).

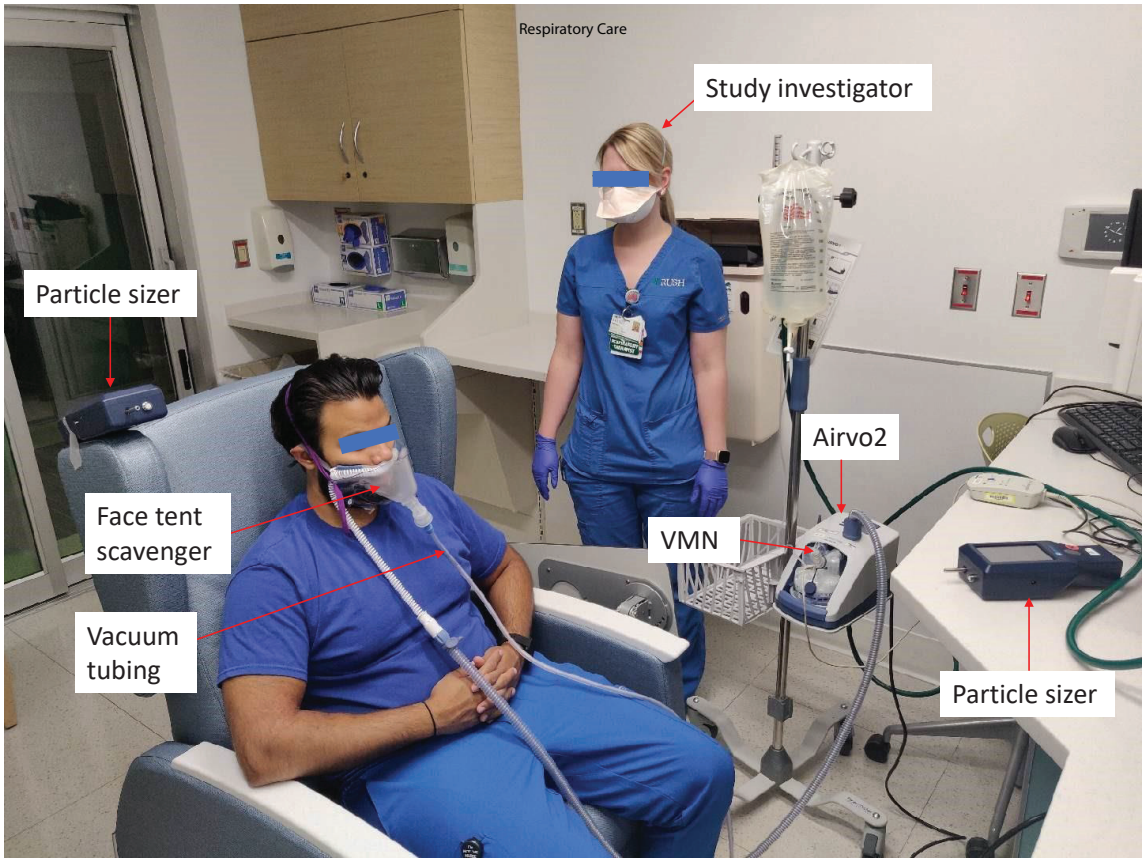
Wearing a surgical mask over nasal cannula during trans-nasal aerosol delivery reduced the fugitive aerosol concentrations to the level of the use of an expiratory filter with a mouthpiece for VMN (Figure 9a) and SVN (Figure 9b).

VMN, vibrating mesh nebulizer; SVN, small volume nebulizer.

Table 1. Inhaled dose of VMN via Vapotherm and Airvo2 at different flow settings.

Flow, L/min	Inhaled dose (%)		p
	Vapotherm	Airvo2	
20	1.3 ± 0.1	12.9 ± 0.9	0.05
40	0.8 ± 0.1	5.0 ± 0.2	0.05
60	NA	3.4 ± 0.1	NA

VMN, vibrating mesh nebulizer; NA, not available (Vapotherm does not operate at 60 L/min).



9 volunteers were recruited and consented

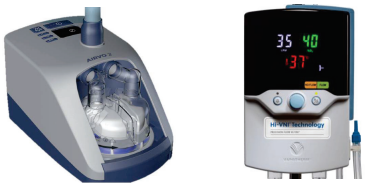
Volunteer and study investigator stayed in the ICU room wearing N95 mask to record baseline aerosol concentration

Volunteer used the following 12 devices and interfaces in a random order: 1) Airvo2 alone, 2) Airvo2 with surgical mask, 3) Airvo2 with scavenger, 4) Airvo2+VMN, 5) Airvo2+VMN with surgical mask, 6) Airvo2+VMN with scavenger, 7) Vapotherm alone, 8) Vapotherm with surgical mask, 9) Vapotherm with scavenger, 10) Vapotherm+VMN, 11) Vapotherm+VMN with surgical mask, 12) Vapotherm+VMN with scavenger. Each device will be used for 8-10 mins

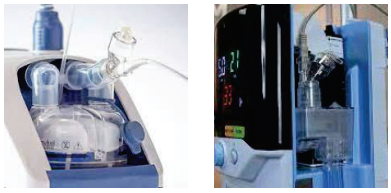
Volunteer and study investigator stayed in the room wearing N95 mask during the 15 mins interval between devices

On a different day, 6 volunteers returned to use the following 6 devices and interfaces in a random order:
1) VMN with a mouthpiece, 2) VMN with a mouthpiece and an expiratory filter, 3) VMN with an aerosol mask, 4) SVN with a mouthpiece, 5) SVN with a mouthpiece and an expiratory filter, 6) SVN with an aerosol mask. Each device will be used for 8-10 mins.

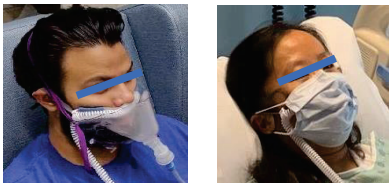
Volunteer and study investigator stayed in the room wearing N95 mask during the 15 mins interval between devices



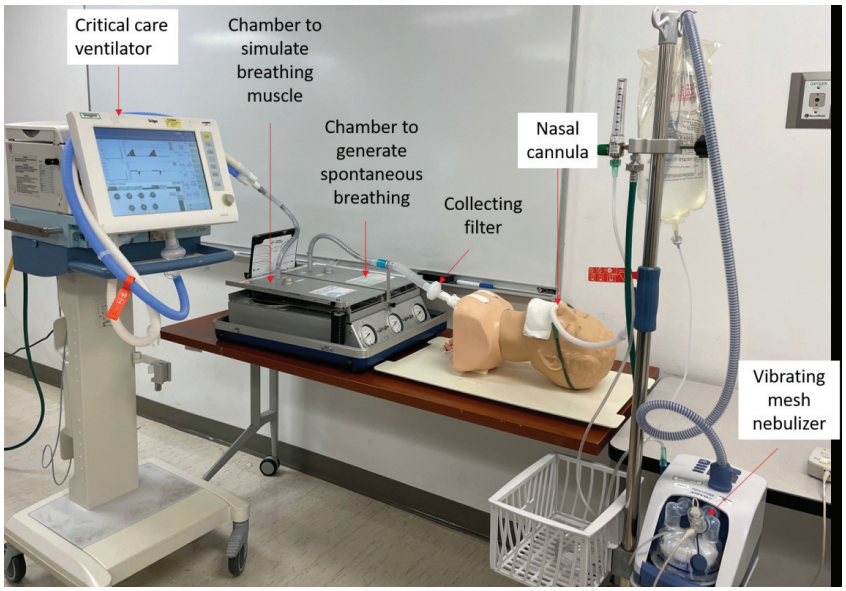
HFNC devices



In-line placement of VMN



Mitigation devices



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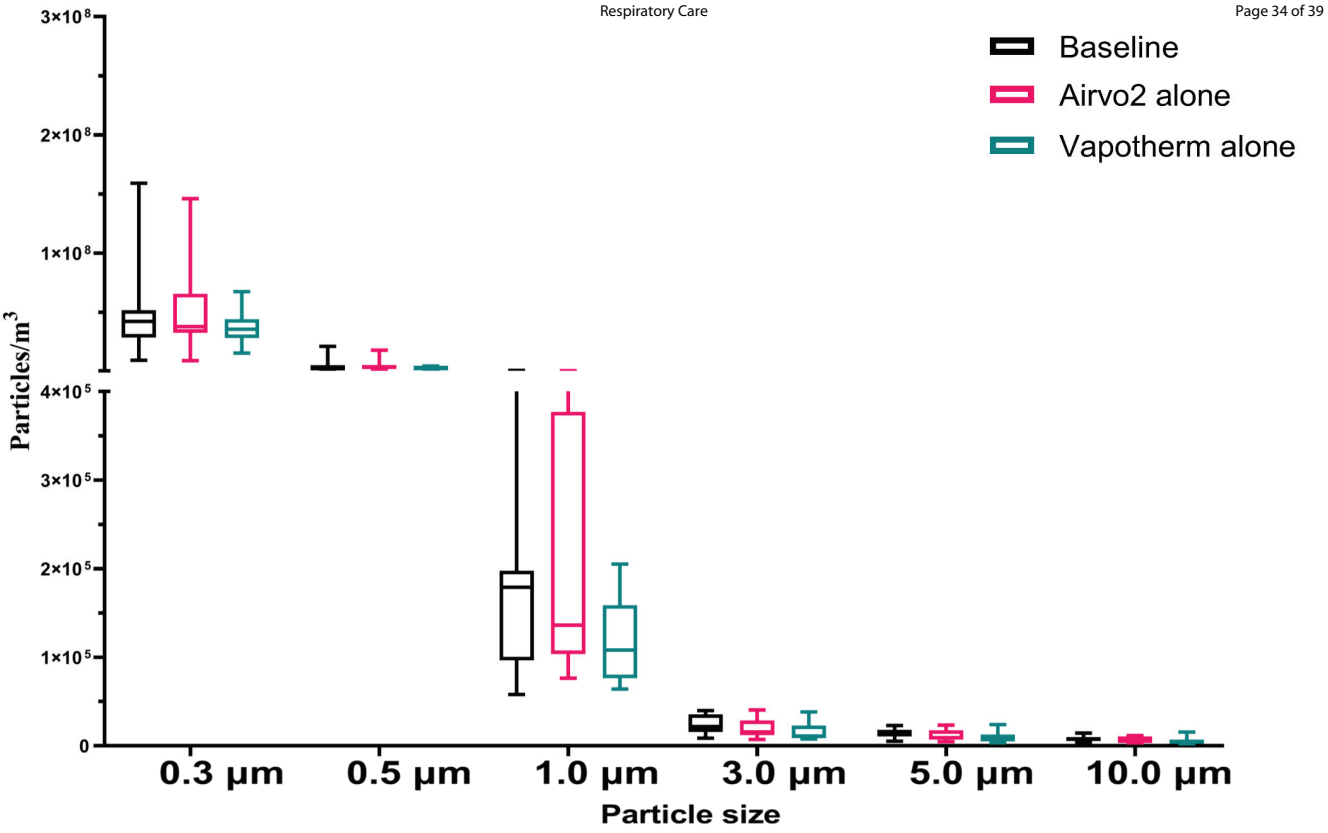

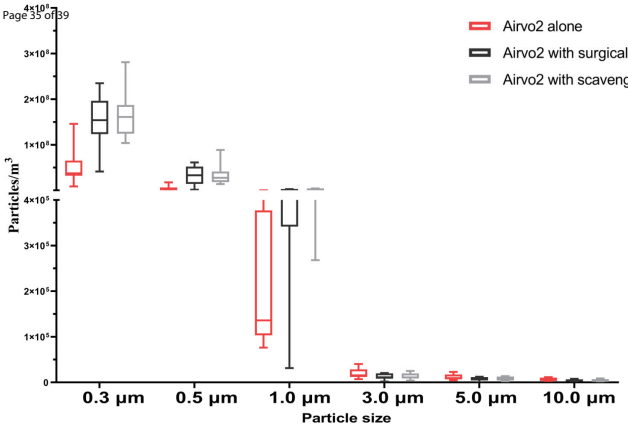

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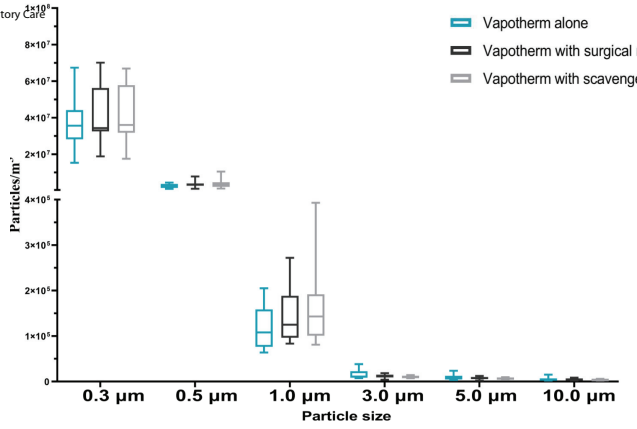

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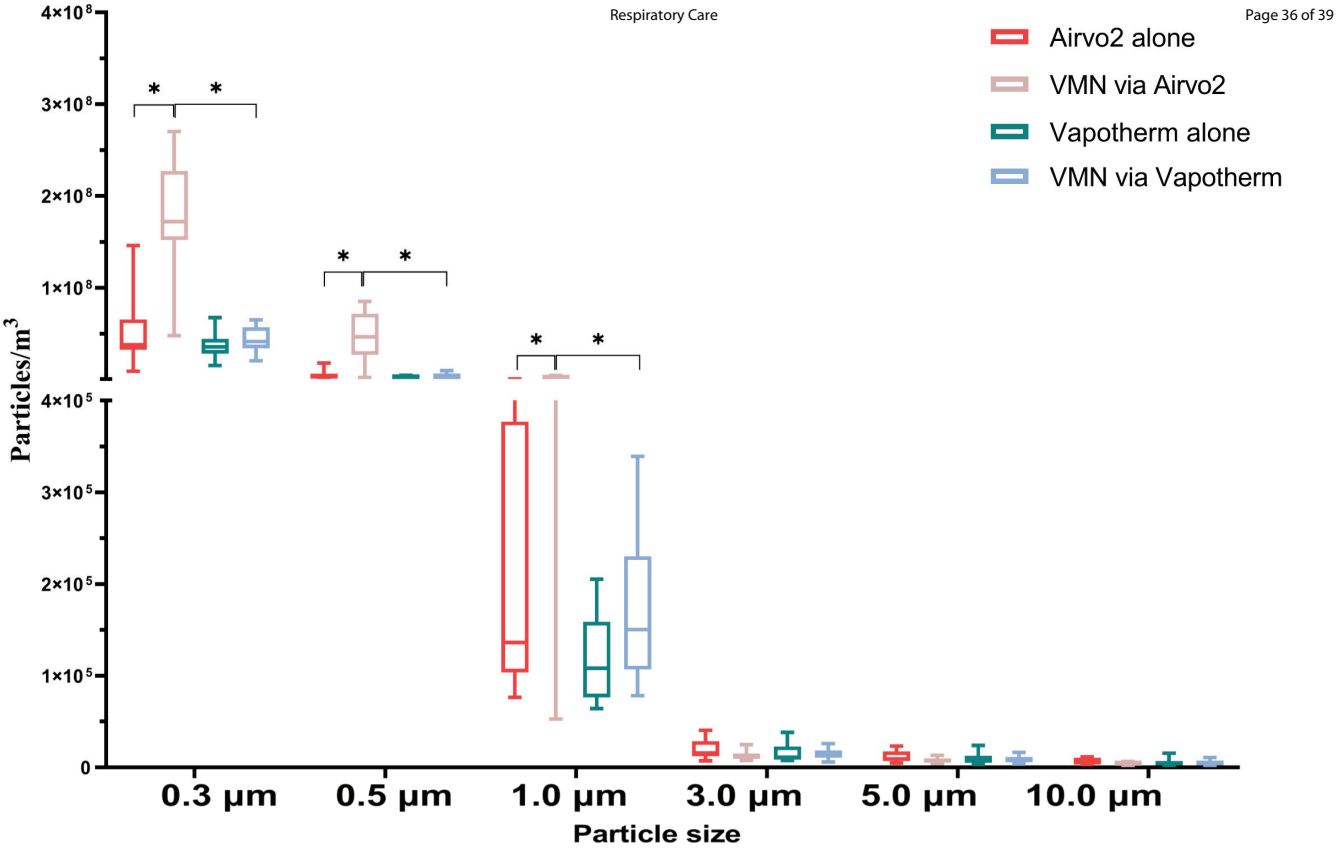

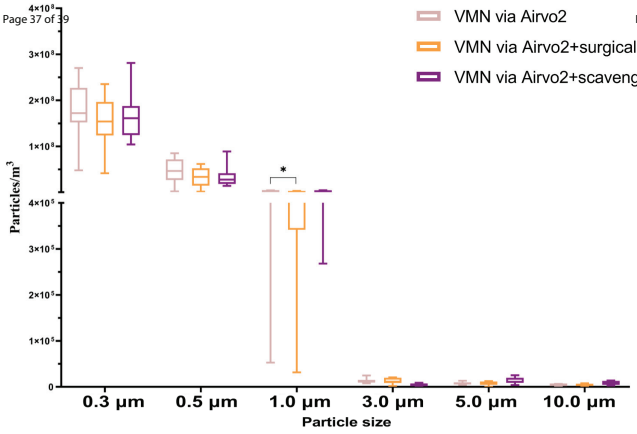

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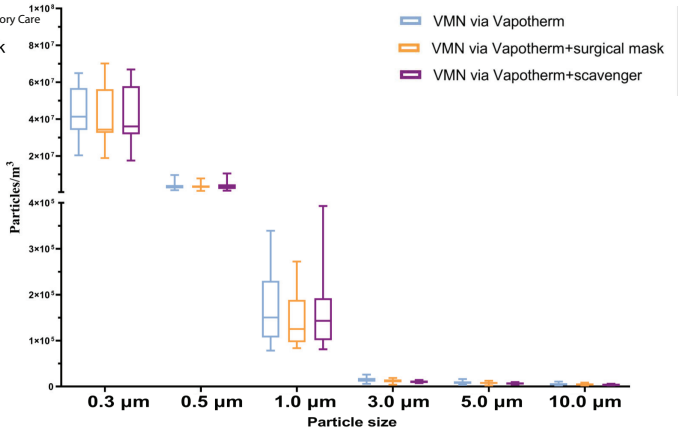

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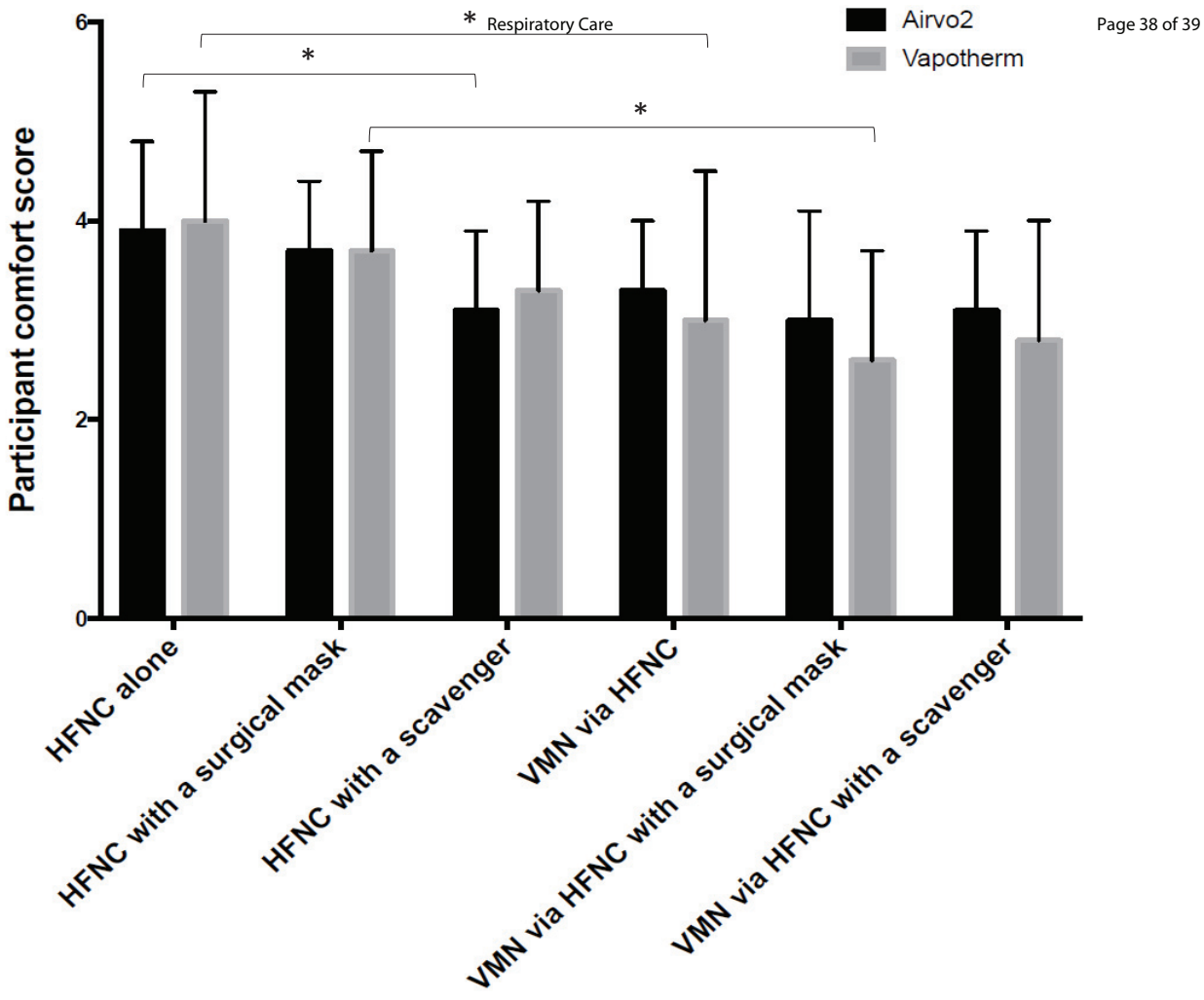

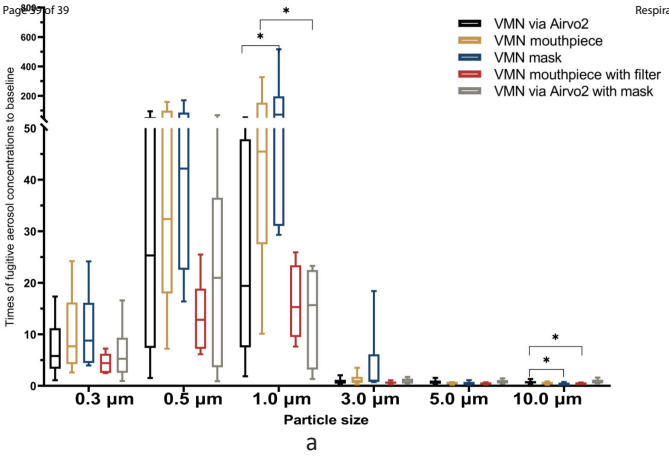

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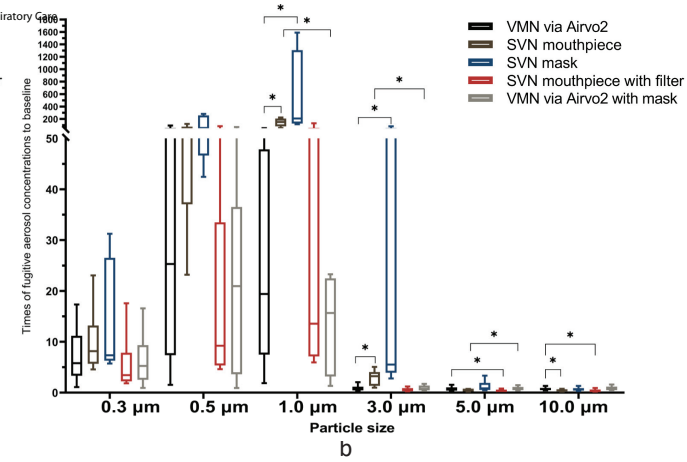

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