Recommended approaches to minimize aerosol dispersion of SARS-CoV2 during noninvasive ventilatory support can deteriorate ventilator performances: a benchmark comparative study Running head: COVID19-specific montage alters ventilator performances

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Recommended approaches to minimize aerosol dispersion of SARS-CoV2 during noninvasive ventilatory support can deteriorate ventilator performances: a benchmark comparative study

Running head: COVID19-specific montage alters ventilator performances

Maxime Patout MD PhD[1,2,3,4], Emeline Fresnel PhD[4,5], Manuel Lujan MD PhD[6], Claudio Rabec[7,8] MD, Annalisa Carlucci MD PhD[9,10], Léa Razakamanantsoa MD[4], Adrien Kerfourn PhD[4,5] Hilario Nunes MD PhD[3,11], Yacine Tandjaoui-Lambiotte MD [11,12], Antoine Cuvelier MD PhD[5], Jean-François Muir MD PhD[4,8], Cristina Lalmoda MD[6], Bruno Langevin MD[13], Javier Sayas MD PhD[14], Jesus Gonzalez-Bermejo MD PhD[2,15], Jean-Paul Janssens MD [16] on behalf of the SomnoNIV group

1. AP-HP, Groupe Hospitalier Universitaire APHP-Sorbonne Université, site Pitié-Salpêtrière, Service des Pathologies du Sommeil (Département R3S), F-75013 Paris, France
2. Sorbonne Université, INSERM, UMRS1158 Neurophysiologie Respiratoire Expérimentale et Clinique, F-75005 Paris, France
3. Respiratory Department, Avicenne Hospital, AP-HP, Bobigny, France
4. Normandie Univ, UNIRouen, EA3830-GRHV, Institute for Research and Innovation in Biomedicine (IRIB), Rouen, France
5. Kernel Biomedical, Bois-Guillaume, France
6. Pneumology Department, Corporació Sanitaria Parc Taulí, Sabadell, Barcelona, Spain
7. Pulmonary Department and Respiratory Critical Care Unit, University Hospital Dijon, Dijon, France.
8. Fédération ANTADIR, Paris, France
9. Pulmonary Rehabilitation Instituti Clinici Scientifici Maugeri-Pavia-Italy
10. Department of Medicine University of Insubria Varese-Como, Italy
11. INSERM U1272 “Hypoxia & the Lung”, Paris 13 University, Bobigny, France
12. Intensive Care Unit, Avicenne Hospital, AP-HP, Bobigny, France
13. Réanimation, Pôle soins aigus, Centre Hospitalier Alès, Alès, France.
14. Servicio de Neumología, Hospital Universitario 12 de Octubre, Madrid, España

15. AP-HP, Groupe Hospitalier Universitaire APHP-Sorbonne Université, site Pitié-Salpêtrière, Service de Pneumologie, Médecine Intensive et Réanimation (Département R3S), F-75013 Paris, France
16. Division of Pulmonary Diseases, Geneva University Hospitals (HUG), Switzerland; Faculty of Medicine, University of Geneva, Switzerland

Corresponding author

Dr. Maxime Patout
AP-HP, Groupe Hospitalier Universitaire APHP-Sorbonne Université, site Pitié-Salpêtrière, Service des Pathologies du Sommeil (Département R3S) Paris, France
47-83 boulevard de l'hôpital,
75013, Paris, France
maxime.patout@aphp.fr

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Abbreviation list

CPAP: continuous positive airway pressure
HME: heat and moisture exchange
IQ: interquartile
NIV: noninvasive ventilation
PEEP: positive end-expiratory pressure
PTP: pressure time product
sPVA: simulated patient-ventilator asynchrony
Vt: tidal volume
WOB: work of breathing

Abstract

Background: SARS-CoV-2 aerosolization during noninvasive positive pressure ventilation may endanger healthcare professionals. Various circuit setups have been described in order to reduce virus aerosolization. However, these setups may alter ventilator performances.

Research question: What are the consequences of the different suggested circuit setups on ventilator's efficacy during continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV)?

Study Design and Method: Eight circuit setups were evaluated on a bench made of a 3-D printed head and an artificial lung. Setups were a dual-limb circuit with an oro-nasal mask, a dual-limb circuit with a helmet interface, a single-limb circuit with a passive exhalation valve, three single-limb circuits with custom-made additional leaks and two single-limb circuits with active exhalation valves. All setups were evaluated during NIV and CPAP. The following variables were recorded: the inspiratory flow preceding trigger of the ventilator, the inspiratory effort required to trigger the ventilator, the triggering delay, the maximal inspiratory pressure delivered by the ventilator, the tidal volume (V_t) generated to the artificial lung, the total work of breathing (WOB) and the pressure time product to trigger the ventilator (PTPt).

Results: With NIV, the type of circuit setup had a significant impact on inspiratory flow preceding the trigger of the ventilator ($p<0.0001$), the inspiratory effort required to trigger the ventilator ($p<0.0001$), the triggering delay ($p<0.0001$); the maximal inspiratory pressure ($p<0.0001$), the V_t (p:0.0008), the WOB ($p<0.0001$), the PTPt ($p<0.0001$). Similar differences and consequences were seen with CPAP as well as with the addition of bacterial filters. Best performance was achieved using a dual limb circuit with an oro-nasal mask. Worst performance was achieved using a dual-limb circuit with a helmet interface.

Interpretation: Ventilator performance is significantly impacted by the circuit setup. The use of dual-limb circuit with oro-nasal masks should be used preferentially.

Introduction

Patients with severe SARS-CoV-2 infection can receive respiratory support using high-flow nasal therapy, continuous positive airway pressure (CPAP) [1] or non-invasive ventilation (NIV) [2]. The use of these treatments is associated with virus aerosolization [3] which may endanger caregivers [4,5]1. For high-flow therapy, surgical masks worn by patients can limit aerosolization [6,7]. During NIV or CPAP, surgical masks cannot be worn. NIV and CPAP are usually delivered to patients using an interface with a built-in intentional leak to avoid carbon dioxide re-breathing. Various strategies have been suggested by experts in order to minimize the risk of aerosolization [5,8]. For CPAP and NIV, the use of non-vented masks with the addition of another bacterial filter on the circuit has been suggested [9] in order to limit aerosolization during expiration. These changes have been implemented using different circuit setups.

If reducing the risk of aerosolization is a priority in the management of patients with SARS-CoV-2 infection, we still need to deliver the best care possible to our patients. The addition of a second bacterial filter in NIV/CPAP circuit is not the standard of care except when dual-limb circuit are used. The addition of these filters may impact on the resistance of the circuit and increase patient's work of breathing. It may also alter ventilator performance and generate patient-ventilator asynchrony which have a deleterious impact in acute respiratory failure [10,11].

Our hypothesis was that the use of these modifications on NIV/CPAP circuits altered ventilator performances. Our aim was to assess the consequences of the different suggested circuit setups for the management of SARS-CoV-2 infected patients on ventilator efficacy during CPAP and NIV.

Study Design and Methods

Experimental model

We used a 3-D printed head mimicking human upper airways and trachea (Online supplement (OLS), e-Figure 1). The 3-D printed head was designed using Zbrush 2019 (Pixologic, CA, USA) by Phoenix Effect Studio (Rouen, France). The model was then printed using 3D-printers Raise3D Pro 2 et Raise3D Pro 2 plus (Raise3D, CA, USA). The model had a dead space of 152 mL and a resistance of 2.4 cmH_2O.

We applied a non-vented oro-buccal mask (Quattro FX, ResMed, San Diego, CA, USA) on the head and verified adequate fitting of the mask before each maneuver. We assessed one setup using a helmet interface. In that case, we used a DimAirLine, NIMV 6R ZIT mask (Dimar, Medolla, Italy). Circuit setups were evaluated with heat and moisture exchange (HME) filters (Inter-term, Intersurgical, Wokingham, United Kingdom), with low-resistance bacterial filters (Iso-guard, Gibeck, Morrisville, NC, USA) or without any filter. Eight circuit setups were evaluated during NIV and CPAP (Figure 1). Setup 4 used a 3D-printed piece designed by MP, EF and JGB for this purpose and freely available (e-Figure 2 - http://www.kernelbiomedical.com/3dleak). With CPAP, we analyzed a 9th setup using a Boussignac CPAP (Vygon, Ecouen, France). The Boussignac setup was only assessed using one circuit setup but with the two-filter configuration.

The trachea was connected to an artificial lung (ASL-5000, Ingmar Medical, Pittsburgh, PA, USA). Respiratory effort was simulated, with a drop in airway pressure at 100 ms (or P0.1) of 5 cmH_2O and a breathing frequency of 30 bpm. This setting was chosen to match the respiratory mechanics seen during SARS-CoV2 infections. The shape of the effort curve was a double exponential. This effort was combined with three different lung mechanics conditions, reflecting the pulmonary function of the simulated patients by modulating resistance (R) and compliance (C) parameters. We simulated a normal lung condition with R = 5 $cmH_2O/l.s$ and C = 60 ml/cmH_2O, during 20 cycles according to measurements performed in patients with severe SARS-CoV-2 infection [12]; a restrictive lung condition with R = 5 $cmH_2O/l.s$ and C = 30 ml/cmH_2O, during 15 cycles and an obstructive lung condition with R = 25 $cmH_2O/l.s$ and C = 60 ml/cmH_2O, during 15 cycles.

All experiments were conducted with an Astral 150 ventilator version 0601 (ResMed, San Diego, CA, USA) without active humidification. Ventilator pre-tests were conducted before each experiment. The ventilator was set as follow: inspiratory pressure: 16 cmH_2O, expiratory pressure: 8 cmH_2O, inspiratory time window: 0.8 to 1.4s, rise time: 100ms, trigger sensitivity: high, cycling: 50% of the peak inspiratory flow. With CPAP, the expiratory pressure was set at 8 cmH_2O. These settings were chosen according to the clinical experience of the authors in the management of patients with severe SARS-CoV-2 infection. When CPAP was provided using a Boussignac CPAP (Vygon, Ecouen, France): pressure was generated using 30 L/min of O_2.

Measurements:

Measurements were performed using the flow and pressure curves provided by the artificial lung (e-figure 3).

For each cycle labelled as synchronized during NIV, we computed 7 indicators (Figure 3). We used four indicators to characterize inspiratory trigger. The indicators were: triggering delay (ms) which measured the time lag between the beginning of simulated effort and the onset of pressure support, flow to trigger (L/min) defined as the value of patient flow measured at the onset of support pressure, pressure to trigger (cmH_2O) defined as the value of muscular pressure P_{mus} measured at the onset of support pressure and inspiratory pressure-time product (PTPt) ($cmH_2O.s$) defined as the area under the pressure-time curve between the onset of inspiratory effort and the return to the set positive end-expiratory pressure (PEEP) as described [13]. We used three indicators to characterize pressurization. The indicators were: delivered inspiratory pressure (cmH_2O) defined as the peak pressure reached during the inspiratory pressurization phase, tidal volume (ml) defined as the difference between the maximal volume delivered within the current cycle to the mechanical lung and the residual volume and total work of breathing of the system (WOB) (mJ) defined as the sum of the patient WOB (integral of muscular pressure x flow product preceding the onset of ventilatory support) and ventilator WOB (integral of airway pressure x flow product between onset of support and instant when 95% of the IPAP level is reached during pressure rise time).

For each cycle labelled as asynchronized during NIV, we characterized the “simulated patient” ventilator asynchrony events (sPVA) according to the framework proposed by the SomnoNIV group [14,15]. We distinguished rate asynchronies from intracycle asynchronies. Rate asynchronies were defined as a mismatch between ventilator and patients' rates. We identified: ineffective efforts when an inspiratory effort was not assisted by the ventilator (*ie.* a drop of airway pressure associated with an increase or decrease of airflow occurring during expiratory or inspiratory phase respectively), double triggering when two mechanical cycles were triggered by the patient, separated by a very short expiratory time (< 30% of mean inspiratory time) and auto-triggering when mechanical cycles were unrelated to patient's spontaneous breathing. Rate intracycle asynchronies were defined as a distortion of the flow and pressure curves during inspiration and/or expiration. We identified premature cycling when the end of the mechanical insufflation preceded the end of patient's inspiration and delayed cycling mechanical insufflation exceeded the patient's own neural expiration. Each asynchrony event was expressed as a percentage by dividing the number of asynchronous cycles by the total of simulated respiratory cycles.

During CPAP, the depression generated by the patient's inspiratory efforts is detected by the ventilator, which regulates the pressure delivered accordingly. For each cycle breathing cycle, the following indicators were computed (Figure 3): regulation delay (ms) which measured the time lag between the start of simulated effort and the onset of pressure regulation, flow to regulation (L/min) corresponding to the flow preceding the ventilator pressurization response, inspiratory pressure-time product (PTPt) ($cmH_2O.s$) defined as the area under the pressure-time curve between the onset of inspiratory effort and the onset of pressure regulation, the maximal delivered pressure (cmH_2O) defined as the peak pressure reached during the current cycle and tidal volume (ml) defined as the difference between the maximal volume delivered within the current cycle to the mechanical lung and the residual volume.

Statistical analysis

Results are expressed as median and interquartile. Chi-square tests were used to compare categorical variables. Kruskal-Wallis tests were used for comparison on continuous variables. Dunn's correction was applied for multiple comparisons. When assessing the impact of a filter, we compared the absence of filter to each filter type as well as the low resistance filter to HME filter. When assessing the impact of circuits, setup 5 was used as reference. All tests were two-sided. For all tests, significance level was set at 0.05. Statistical analysis was performed using Prism 9.0.0 (GraphPad Software, La Jolla, California, USA).

Results

For each setup, 135 respiratory cycles were analyzed with NIV, and 150 with CPAP. Each experiment was conducted with 3 different filter configurations: no filter, low pressure filter or HME filter. In total, 2,430 respiratory cycles were analyzed: 810 (33%) with a normal compliance and resistance profile, 810 (33%) with a low compliance and normal resistance profile and 810 (33%) with a normal compliance and increased resistance profile.

With NIV, the addition of a low pressure and a HME filter had a significant impact on ventilator performance. The addition of a filter (low pressure or HME) was associated with an increase in flow preceding triggering ($p=0.0423$), inspiratory effort to trigger the ventilator ($p<0.0001$), triggering delay ($p<0.0001$), WOB ($p<0.0001$) and PTPt ($p<0.001$) and a decrease in maximal inspiratory pressure ($p<0.0001$), and Vt ($p<0.0001$). Percentage of sPVA was the only parameter for which adding a filter did not cause a significant difference ($p=0.190$; eTable 1). No difference was seen between low pressure and HME filters except for PTPt which was higher using an HME filter ($p=0.0136$) (Table 1 and Figure 4). Similar results were seen with CPAP: albeit for inspiratory flow preceding trigger, all parameters were significantly influenced by the addition of filters. Except for tidal volume, HME filters performed significantly worse than low pressure filters. (Table 1 and Figure 5).

With NIV, the type of circuit setup had a significant impact on in flow preceding triggering ($p<0.0001$), inspiratory effort to trigger the ventilator ($p<0.0001$), triggering delay ($p<0.0001$); maximal inspiratory pressure ($p<0.0001$), V_t (p:0.0008), WOB ($p<0.0001$), PTPt ($p<0.0001$) and sPVA ($p<0.0001$) (Table 2 and Figure 6). Type of sPVA varied significantly between circuit setups ($p<0.0001$) (e-Table 2). Setup 5 using dual limb circuit was the best setup as flow preceding triggering, inspiratory effort to trigger the ventilator, triggering delay, and PTPt were lower than in other setups with similar V_t delivered pressure and sPVA. Setup 8 using a helmet interface had the poorest performance regarding triggering delay, PTPt, inspiratory effort to trigger the ventilator and sPVA. Similar results were obtained with CPAP (Table 2 and Figure 7). With CPAP, the use of setup 8 (helmet) was associated to a significant delay in pressurization and the use of setup 9 (Boussignac CPAP) was associated with higher PTPt values. The maximal delivered inspiratory pressure was significantly lower with the Boussignac setup pressure than the one delivered by ventilators ($p<0.0001$).

Discussion

In this bench-study of different setups proposed for delivering NIV and CPAP during the SARS-CoV-2 pandemic, we have shown that modifying the circuit of a ventilator can impair ventilator triggering, pressurization and performance, and affect work of breathing.

In our study, the use of a dual-limb circuit achieved the best performances. Its use was associated to the lowest inspiratory effort to trigger the ventilator. Therefore, the use of ventilators that allow the use of dual-limb tubing for ventilation should be preferred. Unfortunately, given the burden that the pandemic has put on ventilator supplies, physicians are frequently obliged to use home non-invasive ventilators in order to setup intermediate care facilities [14]. Most of these ventilators can only be used with single-limb circuits. In this case, the addition of intentional leaks (setups 1, 3 and 4) led to a lower maximal pressure without a significant impact on the work of breathing and without increasing sPVA. With CPAP, the use of active expiratory valves (setups 6 and 7) achieved better performance than setups with intentional leaks.

Use of a helmet interface was associated with the worst ventilator performances in this study. This may be explained by the fact that we did not change the ventilator settings. Indeed, helmet interfaces usually require higher pressures than facial or nasal masks [16,17]. Unless the team has expertise in the use of helmets [18,19], we suggest limiting its use to patients who do not tolerate oro-nasal or facial masks or to those for whom adequate fitting of oro-nasal or facial masks cannot be achieved [20]. In this situation, in addition to use higher pressures, we recommend to increase the sensitivity of trigger and cycling settings and to perform a close monitoring of patient-ventilator asynchronies. Indeed, in our simulations, ineffective triggering and late cycling were the most common sPVA identified with the helmet setup (e-Table 2).

Since the beginning of the SARS-COV2 pandemic, NIV and CPAP have been used for the management of acute respiratory failure outside intensive care units [1,4]. In these units, physicians and healthcare associated professionals may be less experienced in the delivery of acute NIV and/or CPAP which may further increase the risk of nosocomial transmission[4]. In this context, in order to limit aerosol generation during NIV/CPAP, we would recommend using the simplest available setup in each organization. This setup may vary between centers. Indeed, this choice needs to take into account: availability of ventilators, availability of additional pieces required for the setup as well as the use of prone positioning outside of ICU [18]. The availability of trained staff to detect and adjust ventilator settings in case of asynchronies is essential to manage patients initiated on NIV or CPAP [21] . We believe that a trained staff, when available, may overcome the limits of circuit setups identified in our bench-tests by personalizing NIV or CPAP settings to patients' requirements.

With the use of single-limb circuits, we did not assess CO_2 re-breathing. However, CO_2 re-breathing is proportional to the dead-space volume between the patient and the exhalation port. Therefore, the exhalation port is usually placed as close as possible to the mask. Given the SARS-CoV-2 pandemic and risk of droplet aerosolization, it has been suggested to connect the filter directly to the mask. Such a strategy increases the dead-space volume. In setups 4 and 6, the filter was placed after the leak. This may therefore limit CO_2 re-breathing with limited droplet aerosolization.

Given the lack of available ventilators during the critical phase of the pandemic, the use of a Boussignac CPAP has been suggested as an alternative. In our study, the Boussignac CPAP achieved lower pressures, and a lower tidal volume for a higher patient inspiratory effort than ventilator-based CPAP. Because of technical limitations, we were unable to increase the flow above 30L/min: a higher flow may have helped to achieve a similar pressure than ventilator-based CPAP.

The level of intentional leakage of each circuit setup may be different: this could have had an impact on ventilator performance. However, in setups 2 and 3, the level of leaks was identical but, on NIV, setup 3 performed better than setup 2. Hence, we hypothesize that the resistance added on the circuit by the second filter is one of the main drivers of the differences seen.

Our results suggest that the use of low-pressure filters had a less deleterious impact than that of HME filters. However, these results need to be interpreted with caution as we ran our tests for a limited period of time and without the impact of humidification coming from air exhaled by the patient. Therefore, in a non-simulated environment, humidity may increase more rapidly the resistance of low-pressure filters than that of HME filters. This may lead to an increase in the work of breathing as well as a decrease in the delivered pressure.

There are a few limitations of our study. Firtsly, we did not assess aerosol dispersion. This would have been difficult to replicate using a bench model. However, with the use of filters, the only meaningful aerosol dispersion that can occur would be related to unintentional mask leaks caused by mask displacement or malposition. Therefore, in addition to the use of dedicated circuit setups, clinicians should carefully choose their CPAP/NIV interface whilst initiating patients with SARS-CoV2 infection on a ventilator. Secondly, this is a bench-model study. We identified significant differences between setups, but we were not able to assess their clinical relevance. However, assessing 8 different setups would have been extremely difficult in clinical practice even using a cross-over design. Thirdly, we did not assess the impact of circuit setup for each of the three lung mechanics simulated (normal, obstructive and restrictive). Fourthly, we could not assess the impact of the different circuit setups on the comfort of patients. As an example, setup 3 may add significant weight to the mask and this may contribute to unintentional leaks, and require further tightening of the mask straps. This setup may also make prone positioning of patient more difficult.

Interpretation

Ventilator performances are affected by the different circuit setups which have been proposed to minimize aerosolization of viral particles during care for SARS-CoV-2 infected patients. The use of dual-limb circuits should be preferred by physicians in order to maintain ventilator performance. If dual-limb circuit ventilators are not available, we suggest using the single-limb setup that is the easiest to provide and monitor in their institution.

References

1. Oranger M, Gonzalez-Bermejo J, Dacosta-Noble P, et al. Continuous positive airway pressure to avoid intubation in SARS-CoV-2 pneumonia: a two-period retrospective case-control study. *European Respiratory Journal* 2020;56(2).

2. Raoof S, Nava S, Carpati C, Hill NS. High-Flow, Noninvasive Ventilation and Awake (Nonintubation) Proning in Patients With Coronavirus Disease 2019 With Respiratory Failure. 2020;158(5):1992–2002.

3. Ahn JY, An S, Sohn Y, et al. Environmental contamination in the isolation rooms of COVID-19 patients with severe pneumonia requiring mechanical ventilation or high-flow oxygen therapy. *J Hosp Infect* 2020;106(3):570–576.

4. Franco C, Facciolongo N, Tonelli R, et al. Feasibility and clinical impact of out-of-ICU noninvasive respiratory support in patients with COVID-19-related pneumonia. *European Respiratory Journal* 2020;56(5).

5. Simonds AK, Hanak A, Chatwin M, et al. Evaluation of droplet dispersion during non-invasive ventilation, oxygen therapy, nebuliser treatment and chest physiotherapy in clinical practice: implications for management of pandemic influenza and other airborne infections. *Health technology assessment (Winchester, England)* 2010;14(46):131–172.

6. Leonard S, Atwood CW, Walsh BK, et al. Preliminary Findings of Control of Dispersion of Aerosols and Droplets during High Velocity Nasal Insufflation Therapy Using a Simple Surgical Mask: Implications for High Flow Nasal Cannula. 2020;

7. Leonard S, Strasser W, Whittle JS, et al. Reducing aerosol dispersion by High Flow Therapy in COVID-19: High Resolution Computational Fluid Dynamics Simulations of Particle Behavior during High Velocity Nasal Insufflation with a Simple Surgical Mask. *J Am Coll Emerg Physicians Open* 2020;

8. Adir Y, Segol O, Kompaniets D, et al. COVID-19: minimising risk to healthcare workers during aerosol-producing respiratory therapy using an innovative constant flow canopy. *European Respiratory Journal* 2020;55(5).

9. Rabec C, Gonzalez-Bermejo J, Respiratory Support, Chronic Care Group GAVO 2 of the French Society of Respiratory Diseases SPLF, GAVO 2 collaborators. Respiratory support in patients with COVID-19 (outside intensive care unit). A position paper of the Respiratory Support and Chronic Care Group of the French Society of Respiratory Diseases. Respir Med Res. 2020;78:100768.

10. Thille AW, Rodriguez P, Cabello B, Lellouche F, Brochard L. Patient-ventilator asynchrony during assisted mechanical ventilation. 2006;32(10):1515–1522.

11. Tonnelier A, Lellouche F, Bouchard PA, L'Her E. Impact of Humidification and Nebulization During Expiratory Limb Protection: An Experimental Bench Study. 2013;58(8):1315–1322.

12. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. Covid-19 Does Not Lead to a “Typical” Acute Respiratory Distress Syndrome. 2020;:rccm.202003–0817LE.

13. Battisti A, Tassaux D, Janssens J-P, Michotte J-B, Jaber S, Jolliet P. Performance characteristics of 10 home mechanical ventilators in pressure-support mode: a comparative bench study. 2005;127(5):1784–1792.

14. Gonzalez-Bermejo J, Perrin C, Janssens JP, et al. Proposal for a systematic analysis of polygraphy or polysomnography for identifying and scoring abnormal events occurring during non-invasive ventilation. 2012;67(6):546–552.

15. Gonzalez-Bermejo J, Janssens J-P, Rabec C, et al. Framework for patient-ventilator asynchrony during long-term non-invasive ventilation. 2019;74(7):715–717.

16. Vargas F, Thille A, Lyazidi A, Campo FR, Brochard L. Helmet with specific settings versus facemask for noninvasive ventilation. 2009;37(6):1921–1928.

17. Pisani L, Mega C, Vaschetto R, et al. Oronasal mask versus helmet in acute hypercapnic respiratory failure. *European Respiratory Journal* 2015;45(3):691–699.

18. Retucci M, Aliberti S, Ceruti C, et al. Prone and Lateral Positioning in Spontaneously Breathing Patients With COVID-19 Pneumonia Undergoing Noninvasive Helmet CPAP Treatment. 2020;

19. Aliberti S, Radovanovic D, Billi F, et al. Helmet CPAP treatment in patients with COVID-19 pneumonia: a multicentre cohort study. *European Respiratory Journal* 2020;56(4).

20. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. *European Respiratory Journal* 2019;53(4).

21. Elliott MW. Non-invasive ventilation: Essential requirements and clinical skills for successful practice. *Respirology* 2019;24(12):1156–1164.

Take-home points:

- Study Question: Are ventilator's performances altered by circuit setups used to limit viral aerosolization of virus?
- Results: Circuits setups and the use of filter significantly impact the performances of ventilators during non-invasive ventilation and continuous positive airway pressure.
- Interpretation: Modifying the circuit of a ventilator can impair ventilator triggering, pressurization and performance, and affect work of breathing.

Table 1: Impact of filters on ventilator performance during noninvasive ventilation and continuous positive airway pressure (HME: heat and moisture exchange, *: p value < 0.05 after correction for multiple comparison when compared to no filter; °: p value < 0.05 after correction for multiple comparison when comparing low-resistance filter and HME filter)

	No filter Median [IQ] / n (%)	**Low resistance filter** Median [IQ] / n (%)	**HME filter** Median [IQ] / n (%)
Non-invasive ventilation			
Flow to trigger (L/min)	11.9 [-12.1 - 23.6]	18.6 [6.5 - 24.3]	19.6 [6.5 - 24]
Inspiratory effort (cmH_20)	-4.91 [-6.95 - -3.94]	-7.43 [-10.27 - -5.64]*	-7.68 [-10.1 - -5.9]*
Time to trigger (ms)	75 [51 - 135]	153 [94 - 307]*	163 [102 - 294]*
Delivered pressure (cmH_2O)	16.7 [16.5 - 16.9]	15.8 [14.5 - 16.2]*	15.6 [14.1 - 16.1]*
Work of breathing (mJ)	537 [317 - 1274]	822 [714 - 1282]*	814 [712 - 1268]*
Tidal volume (ml)	598 [354 - 917]	564 [328 - 760]*	555 [310 - 721]*
Patient ventilator asynchrony	3 (3%)	9 (9%)	8 (8%)
PTPt ($cmH_20.s$)	0.070 [0.040 - 0.130]	0.230 [0.120 - 0.280]*°	0.280 [0.140 - 0.328]*°
Continuous positive airway pressure			
Flow to trigger (L/min)	23.6 [11.5 - 36.9]	25.9 [13.3 - 35.1]	29 [13.7 - 36]
Time to trigger (ms)	220.7 [166 - 262.7]	281.3 [201.2 - 330.1]*°	294.9 [214.8 - 351.6]*°
Delivered pressure (cmH_2O)	8.1 [8.1 - 8.2]	7.9 [7.4 - 8]*°	7.8 [7.1 - 7.9]*°
Tidal volume (ml)	359 [196 - 559]	344 [182 - 485]*°	341 [180 - 469]*°
PTPt ($cmH_20.s$)	0.189 [0.122 - 0.275]	0.328 [0.289 - 0.548]*°	0.382 [0.325 - 0.637]*°

Table 2: Impact of circuit setup on ventilator performance during noninvasive ventilation and continuous positive airway pressure (PTP: pressure time product; NA: not applicable; * : p value < 0.05 after correction for multiple comparison when compared to setup 5)

	Setup 1 Median [IQ] / n (%)	**Setup 2** Median [IQ] / n (%)	**Setup 3** Median [IQ] / n (%)	**Setup 4** Median [IQ] / n (%)	**Setup 5** Median [IQ] / n (%)	**Setup 6** Median [IQ] / n (%)	**Setup 7** Median [IQ] / n (%)	**Setup 8** Median [IQ] / n (%)	**Setup 9** Median [IQ] / n (%)
Non-invasive ventilation									
Flow to trigger (L/min)	23.5 [6.5 - 24.7]*	24.1 [7.9 - 25.3]*	23.2 [7.2 - 24.3]*	24.3 [7.2 - 25.2]*	-11.3 [-15.4 - 7.4]	10.4 [3.7 - 20]*	14.1 [4.1 - 19]*	21.6 [20.1 - 24.7]*	NA
Inspiratory effort (cmH$_2$0)	-7.8 [-10.3 - -5.9]*	-7.7 [-10.3 - -5.8]*	-7.4 [-10.3 - -6.0]*	-7.6 [-10.4 - -6.0]*	-3.9 [-4.4 - -3.5]	-7.3 [-9.7 - -6.0]*	-7.0 [-8.8 - -5.57]*	-10.5 [-11.2 - -9.9]*	NA
Time to trigger (ms)	165 [102 - 312]*	163 [99 - 310]*	153 [104 - 307]*	158 [104 - 320]*	51 [41 - 61]	149 [105 - 266]*	135 [92 - 211]*	323 [278 - 402]*	NA
Delivered pressure (cmH$_2$O)	15.6 [14.6 - 15.7]	15.9 [15 - 16]	13.5 [13.1 - 13.9]*	13.9 [13.6 - 14.4]*	15.6 [15 - 15.9]	16.2 [16.1 - 17.5]*	16.5 [16.4 - 16.5]*	16.3 [15.5 - 16.6]*	NA
Work of breathing (mJ)	823 [717 - 1270]	809 [709 - 1281]	783 [675 - 1320]	780 [686 - 1240]	861 [747 - 1373]	872 [815 - 1046]	520 [301 - 1129]*	875 [766 - 1406]	NA
Tidal volume (ml)	563 [280 - 748]	573 [285 - 780]	535 [267 - 715]*	544 [270 - 732]	553 [325 - 776]	563 [277 - 770]	592 [331 - 949]	529 [512 - 620]	NA
Patient ventilator asynchrony	2 (2%)	6 (7%)	2 (2%)	2 (2%)	2 (2%)	37 (41%)	11 (12%)	38 (42%)	NA
PTPt (cmH$_2$0.s)	0.255 [0.140 - 0.300]*	0.270 [0.130 - 0.300]*	0.260 [0.140 - 0.290]*	0.260 [0.140 - 0.298]*	0.050 [0.040 - 0.060]	0.260 [0.165 - 0.350]*	0.170 [0.150 - 0.290]*	0.640 [0.470 - 1.255]*	NA
Continuous positive airway pressure									
Flow to trigger (L/min)	33.0 [14.3 - 36.6]	33.6 [13.7 - 37.9]	33.2 [14.6 - 37]	33.7 [13.7 - 38]	34.6 [7 - 38.3]	23.2 [8.9 - 25.6]*	23.3 [7.8 - 25.1]*	29.1 [12.2 - 35.1]	NA
Time to trigger (ms)	289.1 [210.9 - 354]	291 [207 - 356]	311.5 [226.1 - 401.4]*	301.8 [214.4 - 379.9]	293.9 [220.2 - 314.5]	194.3 [160.2 - 279.8]*	177.7 [146.5 - 276.4]*	363.3 [265.6 - 404.8]*	NA
Delivered pressure (cmH$_2$O)	7.8 [7.8 - 7.9]*	7.9 [7.9 - 7.9]*	6.8 [6.6 - 6.9]*	7.0 [6.9 - 7.1]*	8.0 [7.9 - 8.1]	7.8 [7.4 - 7.9]*	7.9 [7.8 - 8.2]*	7.9 [7.9 - 8]*	6.5 [6.5 - 6.6]*
Tidal volume (ml)	344 [181 - 474]	345 [182 - 485]*	339 [178 - 461]	340 [180 - 470]	337 [173 - 461]	352 [183 - 526]*	360 [183 - 599]*	339 [182 - 455]	320 [173 - 414]
PTPt (cmH$_2$0.s)	0.353 [0.321 - 0.599]	0.325 [0.297 - 0.552]*	0.478 [0.376 - 0.643]	0.365 [0.325 - 0.59]	0.405 [0.343 - 0.68]	0.312 [0.257 - 0.364]*	0.293 [0.219 - 0.314]*	0.380 [0.322 - 0.863]	0.860 [0.526 - 1.039]*

Figure 1: Setups evaluated in the experiments. (1) mask, filter and right-angle connector in which a 4mm hole has been made (courtesy of CR); (2) mask, filter and a whisper swivel exhalation valve; (3) mask, T-connector, filter and whisper swivel exhalation valve; (4) mask, 3-D printed piece with a 4mm leak, and bacterial filter (courtesy of MP, EF and JGB (e-Figure 2) – 3D model available here: http://www.kernelbiomedical.com/3dleak); (5) mask, dual limb circuit with filter on the inspiratory and expiratory circuits; (6) mask, active expiratory valve and bacterial filter; (7) mask, filter and active expiratory valve; (8) helmet interface, bacterial filter on the inspiratory and expiratory circuits; (9) Boussignac CPAP montage, bacterial filter between valve and mask.

Figure 2: Description of how ventilator performance was assessed during non-invasive ventilation. The onset of pressure support allows to measure the Triggering delay, the Flow to trigger and the Pressure to trigger, and to calculate the inspiratory pressure-time product (PTP_t). The Maximal delivered pressure and the Tidal volume are measured from the ASL 5000 airway pressure and piston volume. The Total Work of Breathing (WOB) corresponds to the checkerboard area (combination of patient and ventilatory work).

Figure 3: Description of how ventilator performances were assessed during continuous positive airway pressure. The onset of pressure regulation allows to measure the Regulation delay, the Flow to regulation and to calculate the equivalent inspiratory pressure-time product (PTPt). The Maximal delivered pressure and the Tidal volume are measured from the ASL 5000 airway pressure and piston volume.

Figure 4: Ventilator performance according to the type of filter used during non-invasive ventilation (HME: heat and moisture exchange, p values are reported when a significant difference after correction for multiple comparison when compared to no filter)

Figure 5: Ventilator performance according to the type of filter used during continuous positive airway pressure (HME: heat and moisture exchange, p values are reported when a significant difference after correction for multiple comparison when compared to no filter)

Figure 6: Ventilator performances during non-invasive ventilation according to the type of circuit setup used (p values are reported when a significant difference after correction for multiple comparison when compared to setup 2)

Figure 7: Ventilator performances during continuous positive airway pressure according to the type of circuit setup used (p value are reported when a significant difference after correction for multiple comparison when compared to setup 2)

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Authors contribution:

MP, EF: conception, acquisition, analysis, interpretation, drafting the work, revising critically

LR: acquisition, interpretation

JPJ, CR, AC, AK, HN, YTL, AC, JFM, CL, BL, JS, TS, JGB, ML: conception, interpretation and, revising critically

Competing Interests statement:

MP reports personal fees from Resmed, Philips Respironics, grants and non-financial support from Fisher & Paykel, nonfinancial support and personal fees from Asten, research grants from B&D Electromedical and Fisher & Paykel, personal fees and non-financial support from Chiesi outside the submitted work.

In the last 2 years JGB received fees from Philips, Resmed, Breas, Lowenstein and Air Liquide for expertise, and a grant from BREAS for a trial, outside the submitted work.

JS reports advisory and teaching payments from ResMed, Philips, Chiesi and Menarini outside the submitted work.

In the last two years, CR received fees from Philips, ResMed, Lowenstein and Fischer & Paykel for expertise, outside the submitted work.

EF, AK, LR, AC, CL, BL, ML, AC, JFM, HN, YTL reports no competing interest

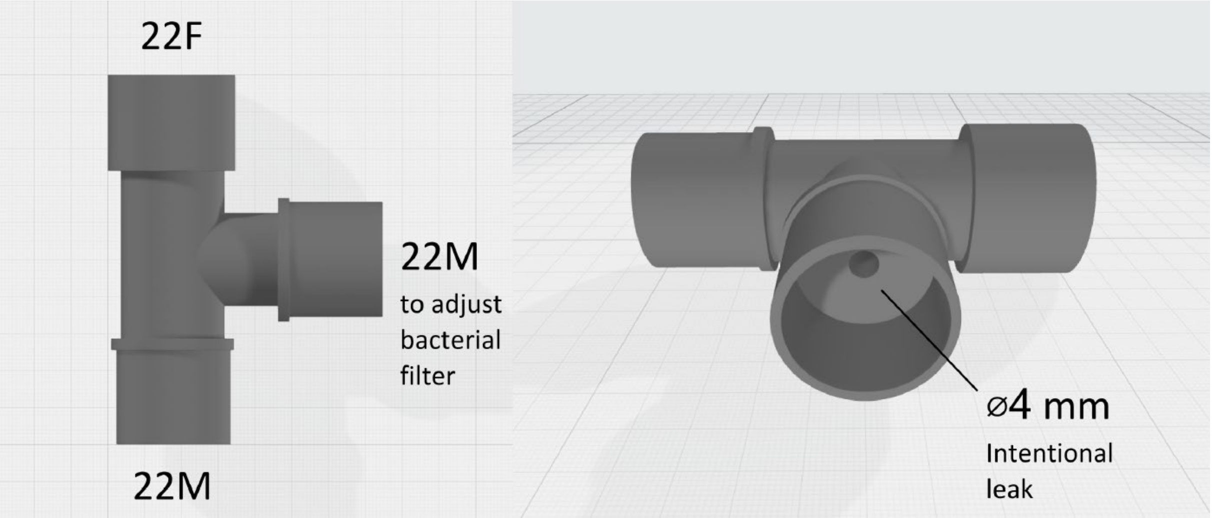
1.

Online supplement of “Recommended approaches to minimize aerosol dispersion of SARS-CoV2 during noninvasive ventilatory support can deteriorate ventilator performances: a benchmark comparative study

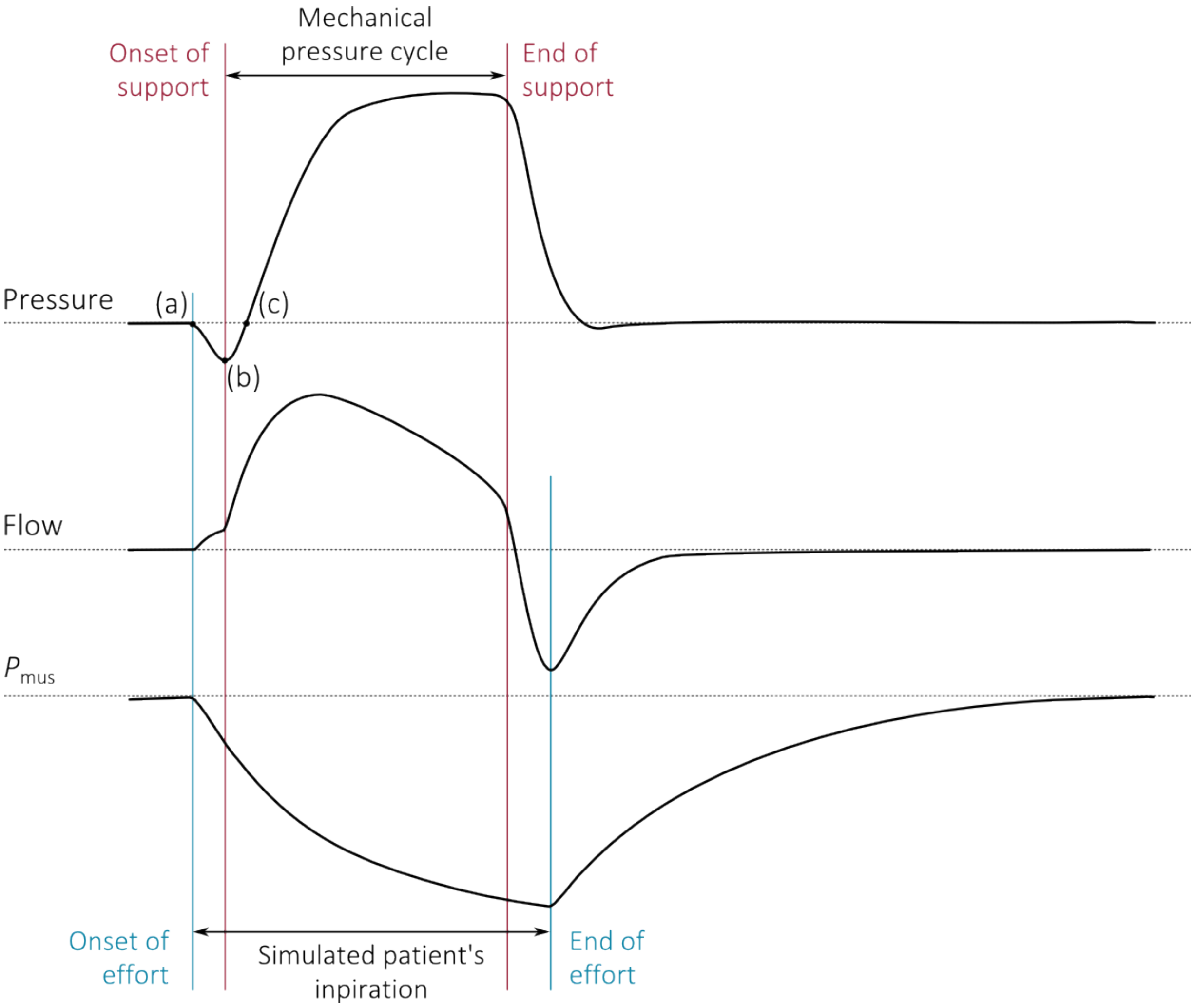
Maxime Patout, Emeline Fresnel, Manuel Lujan, Claudio Rabec, Annalisa Carlucci, Léa Razakamanantsoa, Adrien Kerfourn, Hilario Nunes, Yacine Tandjaoui-Lambiotte, Antoine Cuvelier, Jean-François Muir, Cristina Lalmoda, Bruno Langevin, Javier Sayas, Thomas Similowski, Jesus Gonzalez-Bermejo, Jean-Paul Janssenn on behalf of the SomnoNIV group

e-Figure 1: *3D-printed head model with setup 4 test.*

e-Figure 2: *3-D model of the connector used in setup 4.*



e-Figure 3: *Simulated assisted breathing cycle with ASL 5000 (airway pressure, patient flow and muscular pressure). Point (b) is indicative of the sensitivity of the trigger, while keeping in mind that this value is affected, on one hand, by the intensity of the inspiratory effort and, on the other hand, by the characteristics of the patient-ventilator interface, such as the length of the circuit, its compliance, the presence of a humidifier or the type of mask. In our case, the inspiratory effort and the ventilatory settings are the same in all simulations. Therefore, the only variable for which we assessed the impact on ventilator performances is the circuit setup.*



Experimental model: Circuit setups:

The dead space between the mask and the exhalation valve was*:

- Setup 1: 1 filter + 1 elbow connector (ResMed) ≃ 65 ml
- Setup 2: 1 filter + 1 Whisper Swivel II (Respironics) ≃ 75 ml
- Setup 3: 1 T connector (Intersurgical) + 1 filter + 1 Whisper Swivel II ≃ 105 ml
- Setup 4: 1 3D connector (Phoenix effect) ≃ 25 ml (3-D printed connector available here: http://www.kernelbiomedical.com/3dleak) (efigure 5)
- Setup 6: 1 T connector + 1 expiratory valve (Intersurgical) ≃ 45 ml
- Setup 7: 1 filter + 1 expiratory valve (Intersurgical) ≃ 75 ml

For setups 5 and 8, there was no additional dead space given the dual limb circuit.

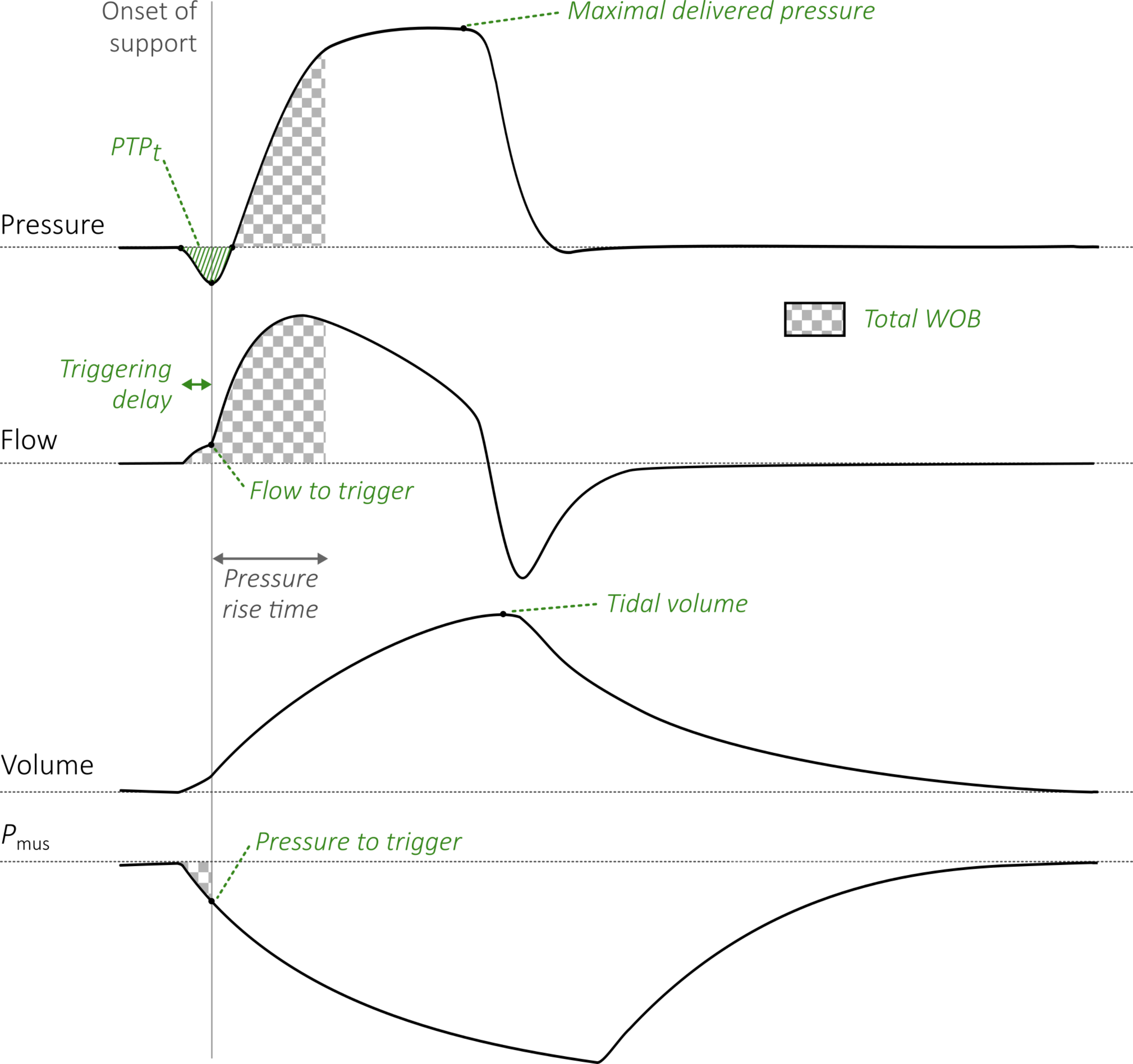
* *an average volume of 50 ml was used for the filter dead space*

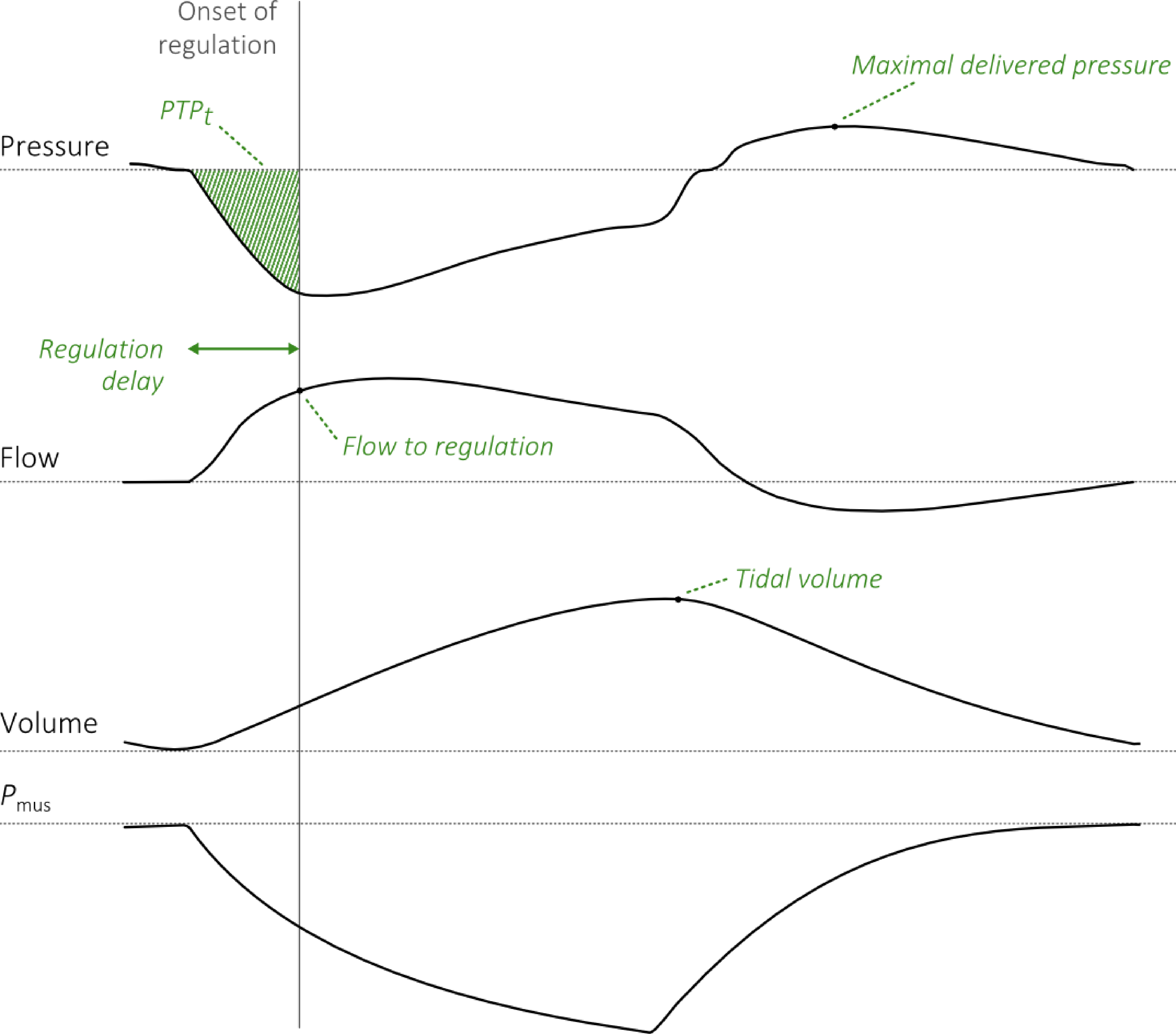
e-Table 1: Proportion of synchronized and asynchronized cycles during non-invasive ventilation without the use of any filter or with the use of low resistance filter (Low filter) and with heat and moisture exchange (HME). Results reported as percentage of cycles (p:0.3240)

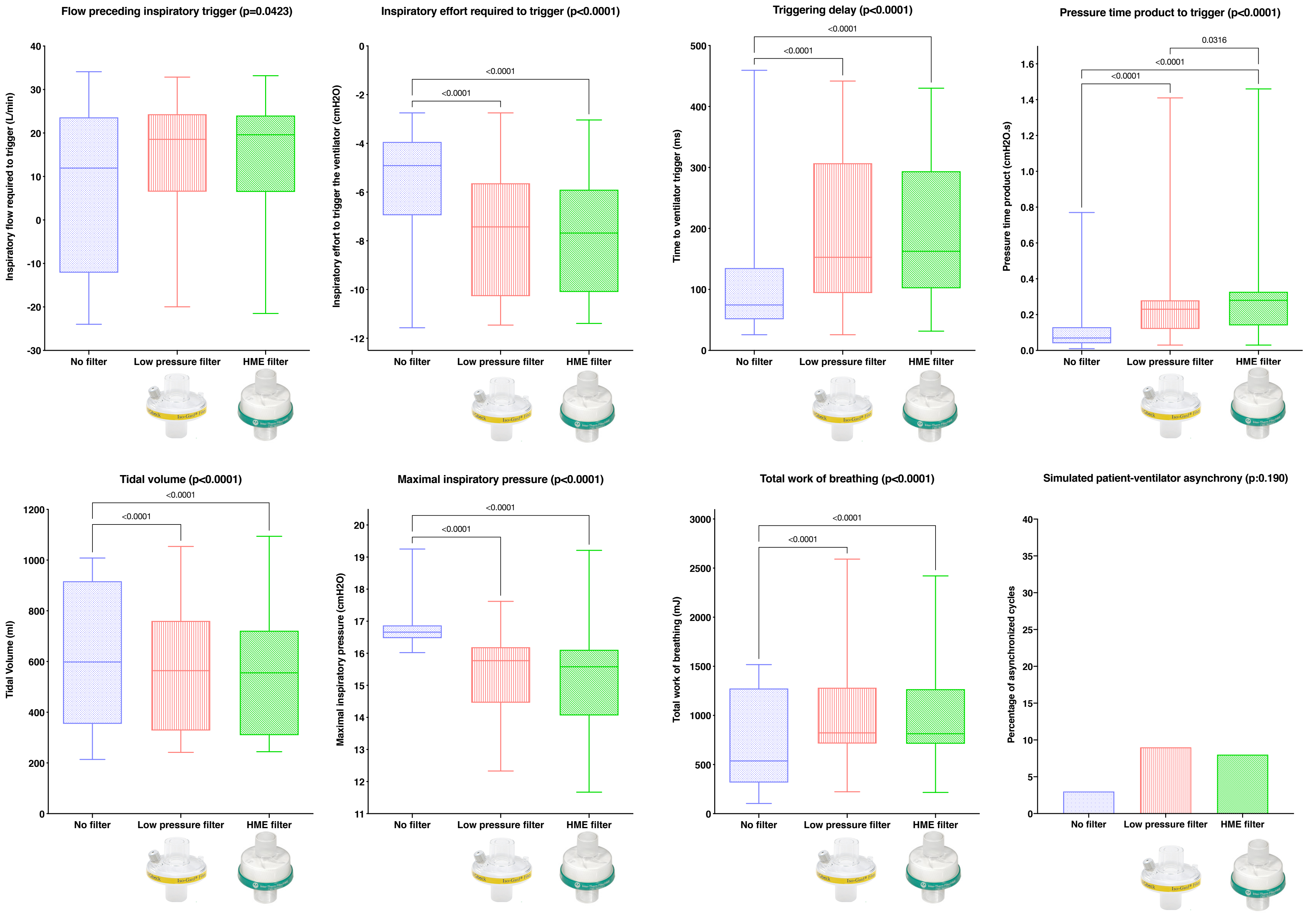
	No filter	**Low filter**	**HME**
Ineffective efforts	1.7	2.5	2.8
Auto-triggering	0.0	1.4	1.7
Double triggering	0.0	0.0	0.0
Early cycling	1.1	0.0	0.0
Late cycling	0.0	5.0	3.3
Synchronized cycles	97.2	91.1	92.2

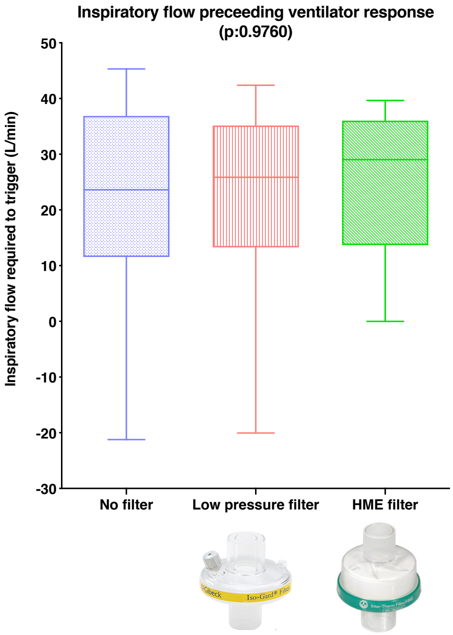
eTable 2: Proportion of synchronized and asynchronized cycles during non-invasive ventilation with the different type of circuit setups. Results reported as percentage of cycles ($p<0.0001$)

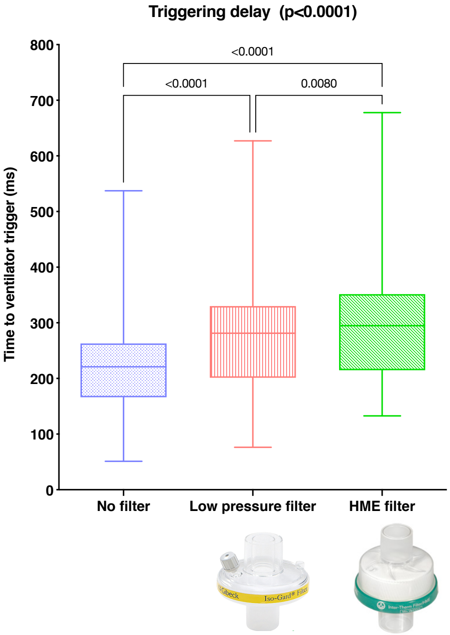
	Setup 1	**Setup 2**	**Setup 3**	**Setup 4**	**Setup 5**	**Setup 6**	**Setup 7**	**Setup 8**
Ineffective efforts	0.0	0.0	0.0	0.0	0.0	5.9	0.0	12.6
Auto-triggering	1.5	1.5	0.0	0.0	1.5	0.7	1.5	1.5
Double triggering	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Early cycling	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.0
Late cycling	0.0	3.0	0.0	0.0	0.0	0.7	0.0	18.5
Synchronized cycles	98.5	95.6	100.0	100.0	98.5	92.6	98.5	64.4

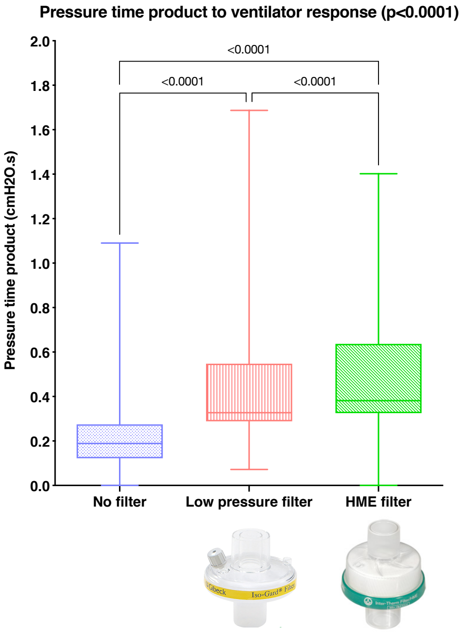

Onset of support
Maximal delivered pressure
PTP$_t$
Pressure
Total WOB
Triggering delay
Flow
Flow to trigger
Pressure rise time
Tidal volume
Volume
P_{mus}
Pressure to trigger

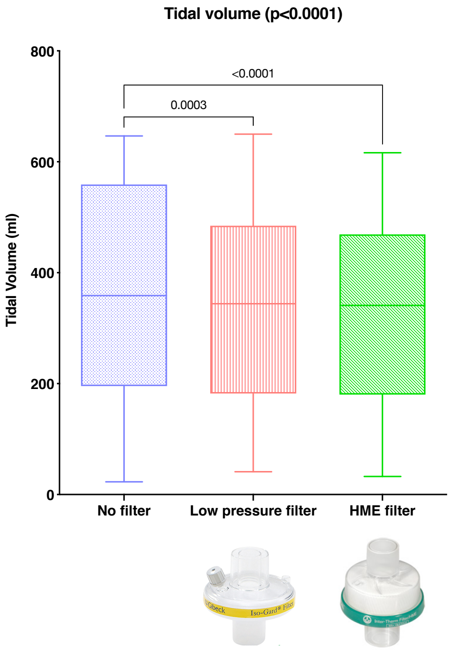

Onset of regulation
PTP$_t$
Maximal delivered pressure
Pressure
Regulation delay
Flow
Flow to regulation
Tidal volume
Volume
P_{mus}

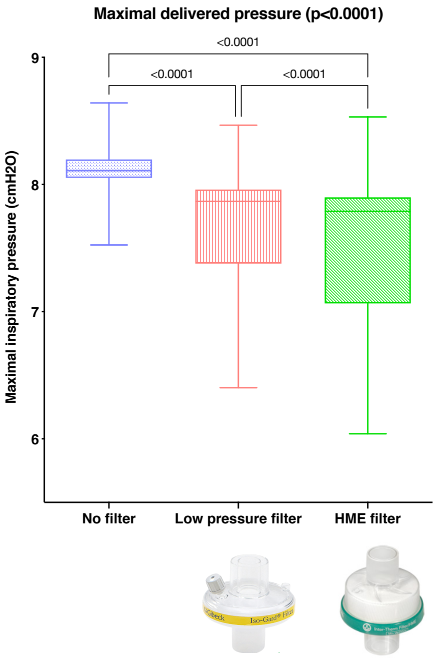

Flow preceding inspiratory trigger (p=0.0423)
Inspiratory flow required to trigger (L/min)
40
30
20
10
0
-10
-20
-30
No filter
Low pressure filter
HME filter
Inspiratory effort required to trigger (p<0.0001)
Inspiratory effort to trigger the ventilator (cmH2O)
0
-2
-4
-6
-8
-10
-12
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Triggering delay (p<0.0001)
Time to ventilator trigger (ms)
500
400
300
200
100
0
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Pressure time product to trigger (p<0.0001)
Pressure time product (cmH2O.s)
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0.0316
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Tidal volume (p<0.0001)
Tidal Volume (ml)
1200
1000
800
600
400
200
0
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Maximal inspiratory pressure (p<0.0001)
Maximal inspiratory pressure (cmH2O)
20
19
18
17
16
15
14
13
12
11
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Total work of breathing (p<0.0001)
Total work of breathing (mJ)
3000
2500
2000
1500
1000
500
0
<0.0001
<0.0001
No filter
Low pressure filter
HME filter
Simulated patient-ventilator asynchrony (p:0.190)
Percentage of asynchronized cycles
40
35
30
25
20
15
10
5
0
No filter
Low pressure filter
HME filter
Iso-Gard® Filter
Inter-Therm Filter

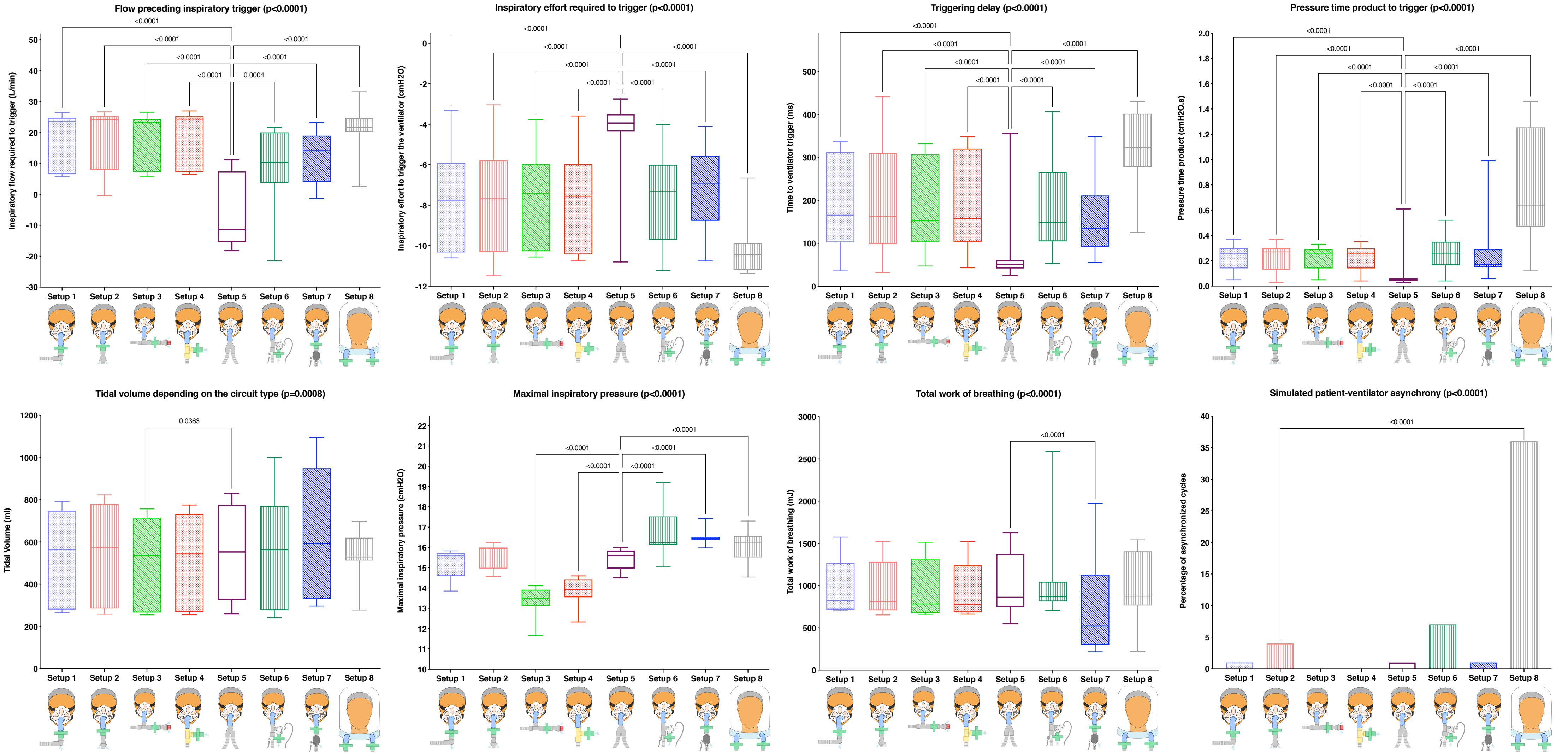

Inspiratory flow preceeding ventilator response (p:0.9760)


Triggering delay (p<0.0001)


Pressure time product to ventilator response (p<0.0001)


Tidal volume (p<0.0001)


Maximal delivered pressure (p<0.0001)



Flow preceding inspiratory trigger (p<0.0001)

Inspiratory effort required to trigger (p<0.0001)

Triggering delay (p<0.0001)

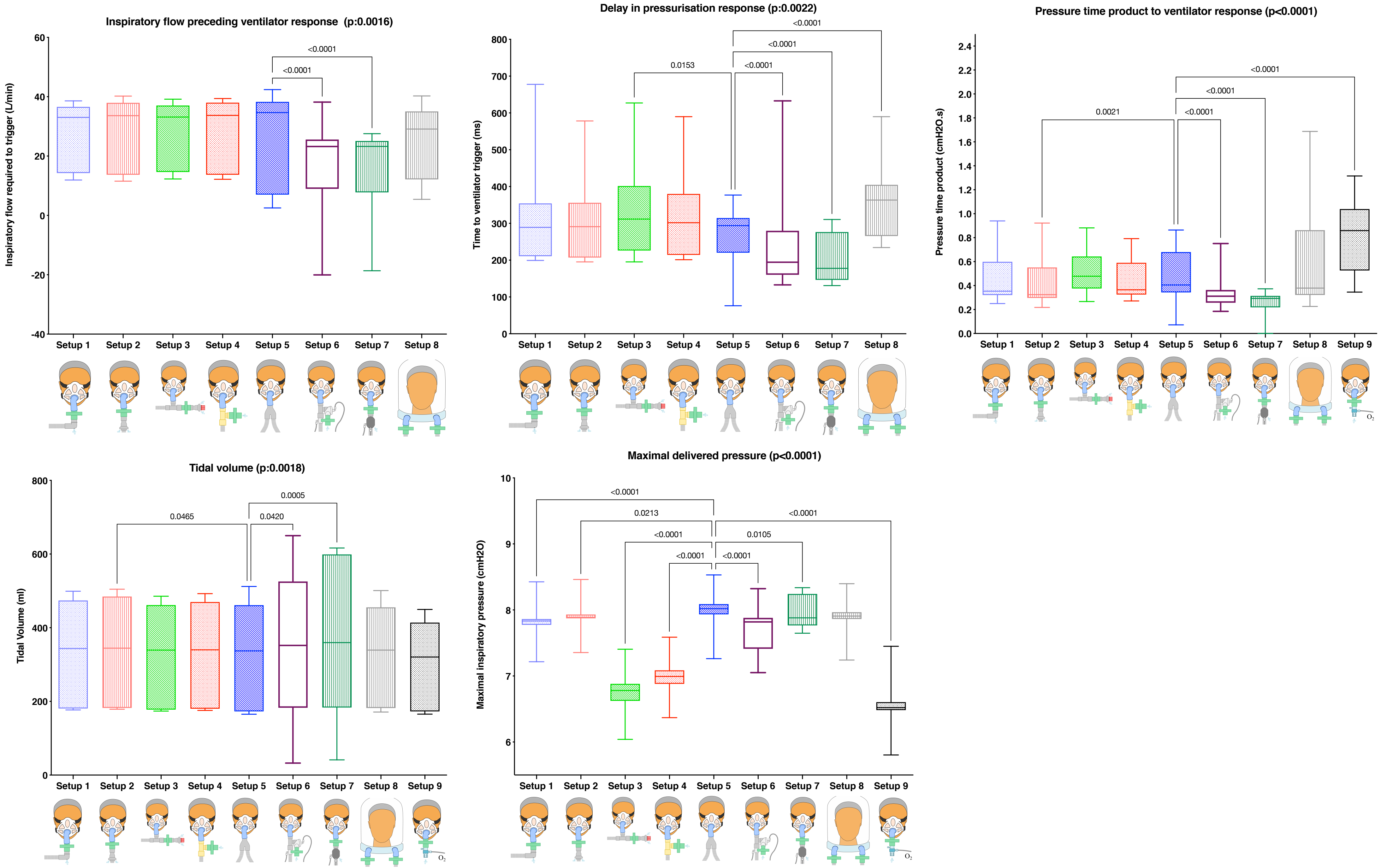
Pressure time product to trigger (p<0.0001)

Tidal volume depending on the circuit type (p=0.0008)

Maximal inspiratory pressure (p<0.0001)

Total work of breathing (p<0.0001)

Simulated patient-ventilator asynchrony (p<0.0001)



Inspiratory flow preceding ventilator response (p:0.0016)

Delay in pressurisation response (p:0.0022)

Pressure time product to ventilator response (p<0.0001)

Tidal volume (p:0.0018)

Maximal delivered pressure (p<0.0001)