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## ► To cite this version:

Mathieu Delorme, Karl Leroux, Antoine Leotard, Ghilas Boussaid, Helene Prigent, et al.. Noninvasive ventilation automated technologies: a bench evaluation of device responses to sleep-related respiratory events. *Respiratory Care*, 2023, 68 (1), pp.18-30. 10.4187/respcare.09807 . inserm-04169660

**HAL Id: inserm-04169660**

**<https://inserm.hal.science/inserm-04169660>**

Submitted on 24 Jul 2023

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## **Noninvasive ventilation automated technologies: a bench evaluation of device responses to sleep-related respiratory events.**

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### **Authors' contributions**

All authors contributed substantially to study conception and design; MD, KL, BL, and FL to data acquisition; MD, BL, and FL to data analysis and interpretation; MD, BL, and FL to drafting the manuscript; and all authors to revising the manuscript for important intellectual content. All authors approved the final version. All authors

agree to be accountable for ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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### **Sources of financial support**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The devices studied were supplied by ASV Santé, a home-care provider involved in the conducting of the current study.

### **Conflict of interest statement**

MD reports personal fees from Air Liquide Medical Systems, personal fees from Breas Medical AB, personal fees from ResMed SAS, non-financial support from L3 Medical, outside the submitted work. Dr. Leotard reports personal fees from Air Liquide Medical Systems, outside the submitted work. Other authors have no conflicts of interest to disclose.

### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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**Number of tables:** 3

**Number of figures:** 5

**Supplementary material:** Yes

**Abstract word count:** 226

**Manuscript word count:** Text: 3485

## ABSTRACT

**Background:** Noninvasive ventilation (NIV) is the reference standard treatment for most situations of chronic respiratory failure. NIV settings must be titrated to both preserve upper airway patency and control hypoventilation. Automatic adjustment of pressure support (PS) and expiratory positive airway pressure (EPAP) may facilitate the initiation and follow-up of domiciliary NIV. However, whether the automatic adjustment algorithms embedded into current devices accurately detect, respond to, and score common sleep-related respiratory events remains unclear.

**Methods:** A bench was set up to simulate central hypopnea (CH), central apnea (CA), obstructive hypopnea (OH), and obstructive apnea (OA). Four home ventilators were evaluated, with their dedicated modes for automatic PS and EPAP adjustment.

**Results:** All four devices increased PS during CH, CA, and OH. However, PS adjustment varied widely in magnitude, with tidal volumes ( $V_T$ ) within  $100\pm 20\%$  of the target being provided by only three devices for CH, one for CA, and one for OH. Two devices increased EPAP for OH and three for OA, including one that also increased EPAP for CA. Only two devices scored residual hypopnea after simulated CA, and only one scored a residual event after OH. One device scored no event.

**Conclusion:** Current NIV devices differ markedly in their responses to, and reporting of, standardized sleep-related respiratory events. Further improvements in embedded NIV algorithms are needed to allow more widespread out-of-laboratory initiation and follow-up of NIV.

**Keywords:** Automated algorithms, Bench study, Chronic respiratory failure, Noninvasive ventilation, Sleep related respiratory events.

## INTRODUCTION

Noninvasive ventilation (NIV) has been shown to improve outcomes of patients with most types of chronic respiratory failure,<sup>1–6</sup> and is currently the standard of care for chronic alveolar hypoventilation.<sup>7–12</sup> Sleep-related respiratory events such as central and/or obstructive apnea and hypopnea affect the efficiency of NIV.<sup>13</sup> NIV settings should therefore be individualized to both control nocturnal hypoventilation and prevent or treat such respiratory events.<sup>14,15</sup>

Polysomnography (PSG) is the recommended method for identifying optimal NIV pressure settings.<sup>16,17</sup> However, patients face long waiting lists for PSG, which is also costly.<sup>18</sup> In addition, the inspiratory and expiratory pressures must strike a compromise between minimizing pressure-related adverse effects on the one hand and preventing upper airway obstruction and/or treating central events during sleep on the other. Needs may change within a given night and from night to night depending on body position, sleep stage, nasal patency, inspiratory muscle efficiency, and other factors, such as the ingestion of alcohol or hypnotic agents that may be used at home.<sup>15</sup>

To replace PSG titration in sleep laboratories, simpler tools allowing remote monitoring of home NIV parameters and residual respiratory events, as well as adjustments of settings, would considerably facilitate the initiation and follow-up of long-term home NIV.<sup>19–22</sup> Manufacturers have developed sophisticated algorithms embedded within NIV devices. These algorithms can automatically adjust basic settings such as expiratory positive airway pressure (EPAP) and pressure support (PS) in response to changes in upper-airway mechanics and airflow.<sup>15,18</sup> However,

these algorithms vary widely across manufacturers, who do not always provide detailed descriptions of them or their updates.<sup>23</sup> For example, some devices adapt their parameters cycle by cycle after identifying an event, whereas others seek to avoid events throughout the NIV session by continuously adjusting the settings even when no events occur. These embedded algorithms will improve care only if they provide good-quality monitoring and setting adjustment.<sup>18,24,25</sup> More data on this point are needed.

We therefore designed a bench study to qualitatively evaluate the appropriateness of automatic setting adjustments by several NIV devices in response to common sleep-related respiratory events. We also assessed the accuracy of device detection and scoring of these events.

## **METHODS**

### ***Bench model***

We used a two-chamber Michigan test lung (MII Vent Aid TTL; Michigan Instruments, Grand Rapids, MI, USA). The driving chamber was connected to, and ventilated by, a dedicated ventilator (Elisee 150, ResMed Ltd, Bella Vista, NSW, Australia), and the experimental chamber was connected to the tested NIV device (Figure 1).

Both chambers were physically connected to each other by a small metal component that allowed the driving chamber to lift the experimental chamber, thereby simulating the spontaneous inspiratory effort, as described previously.<sup>25</sup> The generation of positive pressure in the driving chamber decreased the pressure in the



experimental chamber, triggering a pressure-supported breath. The driving ventilator was in pressure-controlled mode with the following settings: inspiratory pressure, 10 cmH<sub>2</sub>O; positive end-expiratory pressure, 5 cmH<sub>2</sub>O (total inspiratory pressure, 15 cmH<sub>2</sub>O); respiratory rate (RR) 16 breaths/min; and inspiratory time 1.2 s (Inspiration:Expiration ratio, 1:2).

Between the experimental chamber and the tested NIV device, the following were connected in sequence: a parabolic resistor (5 cmH<sub>2</sub>O/L/s) (Pneuflo® Rp5, Michigan Instruments, Grand Rapids, MI, USA), a flow sensor, a collapsible chamber acting as a Starling resistor to allow on-demand partial circuit obstruction,<sup>26,27</sup> a shut-off valve allowing on-demand complete circuit closure, and a pressure sensor (Figure 1). Compliance of the experimental chamber was set at 60 mL/cmH<sub>2</sub>O. The tested NIV devices were connected to the system through a 15-mm circuit and a standard 4-mm diameter intentional leak port. Additional information is provided in the supplementary material.

### ***Devices and ventilatory modes***

We evaluated four ventilators: Vivo 45 (Breas Medical AB, Mölnlycke, Sweden, v. 3.1.4-3.1.4), Prisma VENT40 (Löwenstein Medical Technology, Hamburg, Germany, v. 3.7.00.14), BiPAP A40 Pro (Philips Respironics Inc., Murrysville, PA, USA, v. 1.1.3), and Stellar 150 (ResMed Ltd, Bella Vista, NSW, Australia, v. SX483-0252). All devices were set with their dedicated modes for automatic adjustment of PS based on a prespecified target tidal volume ( $V_T$ ) and of EPAP based on upper airway patency. Automatic calibration of the devices and circuit was performed according to manufacturer recommendations before study data acquisition.

### ***Standardization of settings across devices***

The purpose of this study was to assess the response of each device to standardized respiratory events rather than the accuracy of delivered  $V_T$ . When using ventilatory modes with a set target  $V_T$ , PS is adjusted based on  $V_T$  recorded by the device, as opposed to actual  $V_T$ . However, in several studies, the accuracy of  $V_T$  monitoring differed across devices.<sup>28–32</sup> To overcome this potential source of bias, we standardized the target  $V_T$  settings as follows.

Before each experiment, a baseline run was performed with the target  $V_T$  and PS set to the minimum values available on the devices (300, 100, 200, and 160 mL; and 2, 0, 2, and 0 cmH<sub>2</sub>O, for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively). During this run, ventilation of the experimental chamber was therefore mainly related to the spontaneous respiratory effort generated by the driving ventilator. The  $V_T$  value recorded by the tested device during this run was defined as the baseline  $V_T$ . For all experimental conditions, the target  $V_T$  was then set at 90% of the baseline  $V_T$ , rounded to the nearest 10.

During the baseline runs,  $V_T$  recorded by the device was 360, 270, 320, and 290 mL for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively. Accordingly, during the experiments, target  $V_T$  was 320, 240, 290, and 260 mL for these devices, respectively. Device-recorded  $V_T$  values were used only for this standardization procedure: all  $V_T$  data recorded for the experiments were derived from respiratory flow ( $V'_{aw}$ ) measured by the pneumotachograph.

For all experimental conditions and for each device, the minimum and maximum PS values were 2 and 14 cmH<sub>2</sub>O, respectively, and the minimum and maximum EPAP values were 4 and 14 cmH<sub>2</sub>O, respectively. Table 1 reports the device settings.

### ***Experimental conditions***

For each device, after a 3-minute stabilization period with stable ventilation, four respiratory events were simulated in the following order: central hypopnea (CH), central apnea (CA), obstructive hypopnea (OH), and obstructive apnea (OA). Each event lasted five breaths (about 15-20 s), and events were separated by 1 minute of simulated spontaneous ventilation.

CH was simulated by halving the PS of the driving ventilator and CA by switching the driving ventilator to continuous positive airway pressure (CPAP) mode. For OH, increasing the pressure about the collapsible chamber allowed precise control of its degree of opening with variation of the Starling resistance, thereby simulating upper airway collapse independently from EPAP, to achieve a 50–60%  $V_T$  decrease from the *pre-event* period of stable ventilation to the first respiratory cycle of the OH event. OA was simulated by closing the shut-off valve located between the intentional leak port and the experimental chamber.

Finally, as suggested by reviewers, we performed additional experiments to evaluate whether the duration of the simulated events affected devices responses. We performed CA and OA experiments in which each event lasted 1 minute instead of 15–20 s. For these experiments, the tested devices were switched on and off between the events to ensure that the starting PS and EPAP were similar for CA and OA.

### ***Data acquisition***

$V'_{aw}$  was measured close to the experimental chamber using a pneumotachograph (Fleish #2; Lausanne, Switzerland) connected to a differential pressure transducer (Validyne DP45±2.25 cmH<sub>2</sub>O; Northridge, CA, USA). Airway

pressure ( $P_{aw}$ ) was measured using another pressure transducer (Validyne DP45±56 cmH<sub>2</sub>O) positioned between the shut-off valve and the circuit. The sensors were calibrated according to the manufacturers' recommendations before the experiments. The signals were digitized at 200 Hz using an analog/digital system (MP100, Biopac Systems, Goleta, CA, USA) and recorded on a microcomputer for further analysis. The raw data from the devices were downloaded and analyzed via the manufacturers' dedicated software to identify whether the simulated events were detected and scored.

### **Data analysis**

For each simulated event, three periods of interest were defined: 30 s before the event (*pre-event* period), 15–20 s during the event (event period), and 30 seconds after the event (*post-event* period) (Figure 2). All respiratory cycles during these three periods were included in the analysis. For each respiratory cycle, we determined inspiratory positive airway pressure (IPAP) defined as the maximum  $P_{aw}$  during the inspiratory plateau, EPAP as the mean  $P_{aw}$  during the last 500 ms of expiration, PS as  $IPAP(n) - EPAP(n-1)$ ,  $V_T$  as the integral of flow over time, total cycle time ( $T_{tot}$ ) as the time between two insufflations from the tested device, and RR as  $60/T_{tot}$ .  $V_T$  overshoot was defined as a greater than 20% difference from the mean *pre-event*  $V_T$ .

Detection of an event by the device was defined as the occurrence of an automatic setting adjustment between the *pre-event* and *post-event* periods and/or a scored residual event in the software report. According to current recommendations,<sup>16,33</sup> an appropriate device response to an event was defined as the following changes from the *pre-event* to *post-event* periods: for CH, a PS

increase; for CA, a PS increase combined with backup RR activation; for OH, an EPAP increase combined, when the actual  $V_T$  was below target, with a PS increase; and for OA, as an EPAP increase. When necessary, the manufacturers were contacted to obtain additional information on the device algorithms that might help us understand our findings.

### ***Statistical analysis***

The data are described as mean $\pm$ SD. Most of the results presented are for descriptive purposes only. For instance, the description of the  $V_T$  decrease induced by the simulation of an event (relative to mean *pre-event*  $V_T$ ), or the  $V_T$  reached during the simulation of an event (relative to target  $V_T$ ), did not necessitate using statistical analyses. However, to highlight the adjustment of settings that occurred between the *pre-event* and *post-event* periods, comparisons of variables values during these two periods were performed with the paired-sampled *t*-test. Analyses were performed using Jamovi (version 1.6.15) and *R* (version 4.0.0, *R* Foundation, Vienna, Austria). Two-sided *P* values lower than 0.05 were considered statistically significant.

## **RESULTS**

### ***Consistency of experimental conditions across devices***

Before simulation of the first event, that is, during the first *pre-event* period for CH,  $V_T$  was above target for all four devices (Table 2). Despite this, none of the four devices delivered the set minimum PS. All four devices provided similar PS levels: 2.5 $\pm$ 0.0, 2.6 $\pm$ 0.1, 2.7 $\pm$ 0.0, and 2.8 $\pm$ 0.1 cmH<sub>2</sub>O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively (Table 2). The mean first *pre-event*  $V_T$

calculated from the pneumotachograph data was 360 mL ( $\pm 5\%$ ) for all tested devices (Table 2).

Compared with the mean *pre-event*  $V_T$ ,  $V_T$  during the first cycle of the simulated CH was lower by 39%, 38%, 42%, and 40% for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively. Corresponding decreases were 65%, 70%, 70%, and 67%, respectively, for CA; 53%, 51%, 48%, and 48%, respectively, for OH; and 100% with all devices for OA.

### ***Device responses to the simulated events***

Table 2 reports the responses of each device to the simulated events, and Figures 3 and 4 show the pressure and flow variations recorded for central and obstructive events, respectively. Figure 5 diagrams the dynamic behavior of the devices from the first to the last cycle of each period of interest.

All four devices increased PS during CH, CA and OH. However, the magnitude of the PS increase varied considerably across devices (Table 2 and Figure 5). For CH, all devices except the BiPAP A40 Pro reached  $100\pm 20\%$  of the target  $V_T$  at the last cycle of the event (Figure 5).  $V_T$  overshoot occurred during the first *post-event* cycle with the Vivo 45 (Figure 5A). For CA, only the Prisma VENT40 reached  $100\pm 20\%$  of the target  $V_T$  at the last cycle of the event. The Vivo 45 and BiPAP A40 Pro did not increase PS sufficiently to reach the target  $V_T$  during the event (Figures 5A through 5C). Conversely, the PS increase by the Stellar 150 in response to CA resulted in a  $V_T$  of 148% of the target at the last event cycle and in a  $V_T$  overshoot at the first *post-event* cycle (Figure 5D). For OH, only the Prisma VENT40 increased PS sufficiently to reach  $100\pm 20\%$  of the target  $V_T$  during the event (Figures 5). Both the Prisma VENT40 and Stellar 150 induced  $V_T$  overshoot after the

event (Figures 5B and 5D). For OA, the BiPAP A40 Pro and Prisma VENT40 did not significantly modify PS (Table 2), whereas Vivo 45 and Stellar 150 increased PS during the event, with the latter inducing  $V_T$  overshoot at the first *post-event* cycle (Figure 5D).

All devices activated the backup RR for CA and OA (Figures 5A through 5D). The Stellar 150 increased RR during CA and OA, achieving the target RR (Figure 5D). The Vivo 45 also activated backup RR for OH, inducing asynchronies during the event (Figure 4A).

No device adjusted EPAP for central events, with the exception of the Vivo 45, which increased EPAP in response to CA (Table 2 and Figure 5). Only the Vivo 45 and the Stellar 150 increased EPAP in response to OH (Table 2). All devices except the BiPAP A40 Pro increased EPAP in response to OA. Consistent with its algorithm, BiPAP A40 Pro adjusted EPAP independently of the occurrence of any simulated event (Supplementary Figure 1).

### ***Detection and scoring of the simulated events***

Table 3 reports event detection and the appropriateness of device responses.

Central events induced PS increases with all four devices and were therefore considered detected. For CH, none of the tested devices scored residual events. Although the mean  $V_T$  drop during CA compared with the mean *pre-event*  $V_T$  was 56%, 54%, 62%, and 16% for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively (Figure 3B), only the BiPAP A40 Pro and Stellar 150 scored residual hypopnea in their software reports (Table 3).

OH induced automatic setting adjustments by all four devices and were therefore considered detected. The mean  $V_T$  drop during OH was 62%, 46%, 56%,

and 48% for Vivo 45, Prisma VENT40, BiPAP A40 Pro and Stellar 150, respectively. Only the Stellar 150 scored residual hypopnea in its report (Table 3).

For OA, all devices were considered to have detected the event, based on the occurrence of setting adjustments (Vivo 45, Prisma VENT40, Stellar 150) and/or on appropriate scoring in the device software (Prisma VENT40, BiPAP A40 Pro, Stellar 150).

### ***Effects of event duration and pre-event pressure***

During the 1-minute CA, all four devices increased PS, providing 95%, 127%, 100%, and 103% of the target  $V_T$  at the end of the event for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively. The target  $V_T$  was reached after 18, 5, 11, and 2 cycles for these four devices, respectively.  $V_T$  overshoot at the first *post-event* cycle occurred with all four devices (Supplementary Figure 2A through 2D). During the 1-minute OA, the BiPAP A40 Pro and Prisma VENT40 did not significantly modify PS, whereas the Vivo 45 and Stellar 150 increased PS over the course of the event, with the latter overshooting the  $V_T$  target at the first *post-event* cycle (Supplementary Figure 2D).

All four devices activated backup RR for the 1-minute CA and OA (Supplementary Figure 2A through 2D). The Stellar 150 increased RR during both events, achieving the target RR (Supplementary Figure 2D).

Again, the only device that adjusted EPAP for central events was Vivo 45, which increased EPAP in response to CA (Supplementary Figure 2A). The mean EPAP before the 1-minute OA was  $3.3 \pm 0.0$ ,  $3.4 \pm 0.0$ ,  $3.4 \pm 0.0$ , and  $3.4 \pm 0.0$  cmH<sub>2</sub>O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively. All devices except the BiPAP A40 Pro increased EPAP in response to OA. The EPAP increase from the mean *pre-event* period to the last *post-event* cycle was 1.7, 1.2,



0.0, and 5.4 cmH<sub>2</sub>O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively (compared to 0.9, 1.4, 0.0, and 2.8 cmH<sub>2</sub>O for the 15-20 s OA simulation, respectively).

Despite the longer duration of the events and the comparable *pre-event* EPAP values across devices and between CA and OA, the pattern of EPAP adjustment during the 1-minute events was similar to that of the 15-20 s events (Supplementary Figures 2A through 2D). The scoring of these events by the device software was also the same as for the 15-20 s events.

## DISCUSSION

This bench study demonstrated that automatic responses to simulated sleep-related respiratory events varied considerably across four NIV devices. Moreover, variability also occurred in the device-software reports of events. For all four devices, the responses to the simulated events raise concerns about the appropriateness of automatic adjustments in clinical practice. This finding is somewhat surprising, given the existence of clear recommendations about setting adjustments in response to sleep-related apneas and hypopneas due to central or obstructive mechanisms.<sup>16,33</sup>

We evaluated whether the automatic responses of the devices to events responsible for a  $V_T$  decrease, namely, CH, CA, and OH, were appropriate. To correct a  $V_T$  decrease, PS must be increased. All devices increased PS in these situations and, as such, their responses were appropriate. Although quantitative assessment of the accuracy of delivered  $V_T$ , which has already been evaluated in dedicated bench studies,<sup>28-32</sup> was beyond the scope of the present work, it is worth

noting that differences between the delivered  $V_T$  and the target  $V_T$  were marked and common.  $V_T$  fell below the set target in some cases and, in others, was maintained only at the cost of an overshoot after event termination. These  $V_T$  variations may adversely affect patients, for instance by altering sleep architecture. Achieving the complex balance between efficacy and clinical tolerance is therefore a continuing challenge to manufacturers. Moreover, we did not combine the respiratory events with unintentional leaks, which might have further impaired the ability of the devices to maintain sufficient  $V_T$ .<sup>31,32</sup>

The mean  $V_T$  reduction during simulated CA ranged from 16% to 62%, with only half the devices scoring a residual hypopnea after CA simulation. After OH, a single device scored a residual event, based on a respiratory flow decrease greater than 50% for more than 10 s. These discrepancies across devices are understandable because no formal recommendations exist for scoring hypopneas during NIV.<sup>16,34</sup> In the absence of pulse oximetry and/or arousal detection systems, automatic hypopnea scoring by the device can rely only on flow and pressure variations, resulting in limited sensitivity of hypopnea detection and in variable scoring quality.

Furthermore, NIV is effective only if the upper airway is patent.<sup>16</sup> Three devices appropriately increased EPAP in response to OA, although one also increased EPAP during CA. In contrast to OH, OA cannot be terminated by an EPAP increase, as the intraluminal pressure required to open the completely closed upper airway is substantially higher than that required to prevent complete upper airway closure and is greater than the inspiratory pressure plateau.<sup>35,36</sup> Therefore, automatic adjustment seeks to generate an EPAP just above the upper airway closure pressure once OA is detected then to maintain this level to prevent further occlusion.<sup>14,15</sup> For

OH, only two devices provided an appropriate EPAP response. This finding is of particular concern, given that OH accounts for the vast majority of sleep-related events during NIV in patients with chronic hypoventilation.<sup>13</sup>

An important limitation of this study is that sleep-related respiratory events were simulated for short-term periods. The behavior of the devices may be different over a full night. During the simulated events, low or high velocity of PS changes resulted in under- or over-compensation of  $V_T$ , respectively. The optimal rate of PS adjustment remains unclear but may be related to the time-course of the event responsible for the  $V_T$  decrease.<sup>25</sup> Conceivably, faster adjustment may be required during short-term events, whereas slower adjustment might be more appropriate when compliance decreases due to body position. Furthermore, the BiPAP A40 Pro algorithm is not designed to respond to single events, such as those simulated for our study, but instead continuously assesses airway resistance using the intermittent forced oscillation technique,<sup>37</sup> and adjusts EPAP to prevent events over the full night. In a randomized controlled study, NIV using this algorithm provided similar benefits to standard PS ventilation in patients with obesity hypoventilation syndrome, without altering sleep quality or gas exchange.<sup>38</sup> This finding suggests that our bench study may have underestimated the effectiveness of this device. Nevertheless, our results underline that clinical-trial results have external validity only for the tested device, given the possibility of major differences across devices.<sup>38,39</sup>

## **CONCLUSION**

Current NIV devices differ substantially in their responses to standardized simulated sleep-related respiratory events. Moreover, event recording in software reports also varies considerably. Clinical guidelines for the management of OA

include CPAP titration using automated devices at home.<sup>40</sup> The ability to do the same in patients who require NIV is impatiently awaited. However, to meet this expectation, our results suggest a need for further improvements in algorithms embedded in NIV devices.

## **ABBREVIATIONS**

CA: Central apnea

CH: Central hypopnea

CPAP: Continuous positive airway pressure

EPAP: Expiratory positive airway pressure

IPAP: Inspiratory positive airway pressure

Paw: Airway pressure

PS: Pressure support

PSG: Polysomnography

NIV: Noninvasive ventilation

OA: Obstructive apnea

OH: Obstructive hypopnea

RR: Respiratory rate

V'aw: Respiratory flow

V<sub>T</sub>: Tidal volume

**Acknowledgements:** None.

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## FIGURE TITLES AND CAPTIONS

### Figure 1. Experimental setup.

$V'_{aw}$ , respiratory flow;  $P_{aw}$ , airway pressure.

### Figure 2. Data acquisition and periods of interest.

Example of data recorded during a simulated episode of obstructive apnea. The periods of interest were the 30 seconds preceding the event (*pre-event* period), 15–20 seconds of event duration (*event* period), and 30 seconds following the event (*post-event* period).

$V'_{aw}$ , respiratory flow;  $P_{aw}$ , airway pressure; OA, obstructive apnea.

### Figure 3. Device responses to central hypopnea and apnea.

3A: Central hypopnea

3B: Central apnea.

The dashed vertical lines show the beginning and end of the event period.

$V'_{aw}$ , respiratory flow;  $P_{aw}$ , airway pressure.

### Figure 4. Device responses to obstructive hypopnea and apnea.

4A: Obstructive hypopnea

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Figure 5. Diagram of dynamic device behavior from the first to the last cycle of each period of interest.

Figure 5A: Vivo45 (Breas)

Figure 5B: Prisma VENT40 (Löwenstein)

Figure 5C: BiPAP A40 Pro (Philips)

Figure 5D: Stellar 150 (ResMed)

\*:  $V_T = 294\%$  of target  $V_T$ ;  $226\%$  of mean *pre-event*  $V_T$

PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate;  $V_T$ , tidal volume.

## **QUICK LOOK**

**Current knowledge:** Automatic adjustment of pressure support and expiratory positive

airway pressure may facilitate the initiation and follow-up of home noninvasive ventilation (NIV). However, whether algorithms embedded in current devices accurately detect, respond to, and score common sleep-related respiratory events remain poorly documented.

**What This Paper Contributes To Our Knowledge:** Current NIV devices vary substantially in their responses, and reports of, standardized sleep-related respiratory events. Further improvements in embedded NIV algorithms are needed to allow broader out-of-laboratory initiation and follow-up of home NIV.

**Table 1. Settings for each of the four tested devices**

Device	Vivo 45	Prisma VENT40	BiPAP A40 Pro	Stellar 150
Mode	PSV(TgV) – AE	AutoST +V	AVAPS – AE	iVAPS – AutoEPAP
Target $V_T^*$ ; mL	320	240	290	260
PS (min – max); cmH <sub>2</sub> O	2 – 14	2 – 14	2 – 14	2 – 14
EPAP (min – max); cmH <sub>2</sub> O	4 – 14	4 – 14	4 – 14	4 – 14
RR; breaths/min	12	12	12	16 <sup>‡</sup>
Ti (timed); sec	1.2	1.2	1.2	–
Ti (min – max); sec	0.9 – 1.9	0.9 – 1.9	–	0.9 – 1.9
Rise time <sup>†</sup>	4	2	2	200
Trigger	4	4	4 L/min	Medium
Cycling	7	25%	25%	Medium

**Abbreviations:** VT, tidal volume; PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate; Ti, inspiratory time; PSV(TgV), pressure support ventilation with target VT; AE, auto-EPAP; AutoST +V, automatic spontaneous timed mode with target VT; AVAPS, average volume assured pressure support; iVAPS, intelligent volume assured pressure support.

**Specific settings:**

Breas Vivo 45, EPAP step: 2.0 cmH<sub>2</sub>O.

Löwenstein Prisma VENT40, AutoF: off; Trigger type: manual; Target VT speed: III; deltaP; 12 cmH<sub>2</sub>O;

Expiratory fall time: 2.

Philips BiPAP A40 Pro, AVAPS speed: 5.0 cmH<sub>2</sub>O/min; Trigger type: flow.

ResMed Stellar 150, Height: 175cm; Target Va: 2.3 L/min; Expiratory fall time: 200 ms.

\*: The baseline  $V_T$  monitored by the tested devices during the baseline run (with PS and target  $V_T$  set at the minimum values available on the tested devices) was 360, 270, 320, and 290 mL for the Vivo 45, Prisma VENT40, BiPAP A40 Pro and Stellar 150, respectively. The target  $V_T$  for the experiments was 90% of the baseline  $V_T$ .

†: Rise time was set to provide similar duration between beginning of inspiratory effort and peak inspiratory flow for each device.

‡: The target respiratory rate in iVAPS mode was set at 16 breaths/min to be in line with the spontaneous respiratory rate of the model. With this setting, the backup respiratory rate threshold (below which controlled cycles are generated) is comparable to that of other tested devices (*i.e.*, approximately 12 breaths/min).



**Table 2. Auto-adjustment of settings and tidal volume variations from *pre-* to *post-*event according to the tested devices**

	Central Hypopnea		Central Apnea		Obstructive Hypopnea		Obstructive Apnea	
	Pre-event	Post-event	Pre-event	Post-event	Pre-event	Post-event	Pre-event	Post-event
<b>Vivo 45</b>								
PS (cmH <sub>2</sub> O)								
Mean ± SD	<b>2.5 ± 0.0</b>	<b>3.3 ± 0.9*</b>	<b>2.4 ± 0.0</b>	<b>3.0 ± 0.2*</b>	<b>2.4 ± 0.0</b>	<b>2.8 ± 0.5†</b>	2.4 ± 0.0	2.7 ± 0.4
First cycle – Last cycle	2.5 – 2.5	4.7 – 2.5	2.4 – 2.4	3.3 – 2.9	2.5 – 2.5	3.8 – 2.5	2.4 – 2.4	3.4 – 2.4
EPAP (cmH <sub>2</sub> O)								
Mean ± SD	3.4 ± 0.0	3.3 ± 0.0	<b>3.3 ± 0.0</b>	<b>4.2 ± 0.0*</b>	<b>4.2 ± 0.0</b>	<b>5.1 ± 0.0*</b>	<b>5.1 ± 0.0</b>	<b>5.8 ± 0.3*</b>
First cycle – Last cycle	3.4 – 3.4	3.4 – 3.3	3.4 – 3.4	4.2 – 4.2	4.2 – 4.2	5.1 – 5.1	5.1 – 5.1	5.1 – 6.0
V <sub>T</sub> (mL)								
Mean ± SD	371 ± 6	387 ± 43	<b>346 ± 5</b>	<b>401 ± 40*</b>	343 ± 1	351 ± 20	335 ± 2	341 ± 17
First cycle – Last cycle	375 – 361	454 – 348	335 – 353	370 – 460	342 – 343	388 – 339	338 – 333	382 – 336
<b>Prisma VENT40</b>								
PS (cmH <sub>2</sub> O)								
Mean ± SD	<b>2.6 ± 0.1</b>	<b>2.8 ± 0.4†</b>	<b>2.7 ± 0.0</b>	<b>2.8 ± 0.3†</b>	<b>2.7 ± 0.0</b>	<b>4.7 ± 0.8*</b>	2.7 ± 0.0	2.7 ± 0.1
First cycle – Last cycle	2.6 – 2.5	3.7 – 2.6	2.7 – 2.7	3.6 – 2.6	2.6 – 2.7	6.0 – 3.6	2.7 – 2.8	2.9 – 2.7
EPAP (cmH <sub>2</sub> O)								
Mean ± SD	3.4 ± 0.0	3.3 ± 0.0*	3.3 ± 0.0	3.3 ± 0.0	3.3 ± 0.0	3.3 ± 0.0	<b>3.3 ± 0.0</b>	<b>4.7 ± 0.0*</b>
First cycle – Last cycle	3.4 – 3.4	3.3 – 3.3	3.3 – 3.3	3.3 – 3.3	3.3 – 3.3	3.3 – 3.3	3.3 – 3.3	4.6 – 4.6
V <sub>T</sub> (mL)								
Mean ± SD	352 ± 4	360 ± 23	<b>347 ± 3</b>	<b>360 ± 9*</b>	<b>341 ± 6</b>	<b>430 ± 32*</b>	<b>353 ± 3</b>	<b>339 ± 12*</b>
First cycle – Last cycle	351 – 354	414 – 343	341 – 348	379 – 353	329 – 347	482 – 386	354 – 347	310 – 340
<b>BiPAP A40 Pro</b>								
PS (cmH <sub>2</sub> O)								
Mean ± SD	<b>2.7 ± 0.0</b>	<b>3.2 ± 0.3*</b>	<b>2.6 ± 0.0</b>	<b>3.6 ± 0.1*</b>	<b>2.6 ± 0.0</b>	<b>3.8 ± 0.3*</b>	2.8 ± 0.1	2.7 ± 0.0
First cycle – Last cycle	2.7 – 2.6	3.7 – 2.9	2.6 – 2.7	3.8 – 3.5	2.7 – 2.6	4.2 – 3.5	2.7 – 2.8	2.7 – 2.8
EPAP (cmH <sub>2</sub> O)								
Mean ± SD	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	5.9 ± 0.0	5.9 ± 0.0	8.0 ± 0.0	8.0 ± 0.0
First cycle – Last cycle	3.9 – 3.9	3.9 – 3.9	3.9 – 3.9	3.9 – 3.9	5.9 – 6.0	5.9 – 6.0	8.0 – 8.0	8.0 – 8.0
V <sub>T</sub> (mL)								
Mean ± SD	<b>358 ± 11</b>	<b>364 ± 15*</b>	344 ± 8	345 ± 25	<b>336 ± 3</b>	<b>368 ± 13*</b>	345 ± 5	347 ± 2
First cycle – Last cycle	372 – 344	392 – 353	336 – 355	368 – 333	332 – 334	386 – 345	356 – 341	346 – 346
<b>Stellar 150</b>								
PS (cmH <sub>2</sub> O)								
Mean ± SD	<b>2.8 ± 0.1</b>	<b>3.2 ± 0.6†</b>	<b>2.8 ± 0.1</b>	<b>3.7 ± 1.7†</b>	<b>2.8 ± 0.1</b>	<b>4.2 ± 2.1†</b>	2.7 ± 0.1	<b>8.0 ± 5.4*</b>
First cycle – Last cycle	2.8 – 2.8	4.1 – 2.8	2.8 – 2.9	7.1 – 2.8	2.7 – 2.7	7.9 – 2.7	2.8 – 2.7	14.5 – 3.1
EPAP (cmH <sub>2</sub> O)								
Mean ± SD	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	<b>3.9 ± 0.0</b>	<b>4.4 ± 0.0*</b>	<b>4.4 ± 0.0</b>	<b>5.8 ± 1.2*</b>
First cycle – Last cycle	3.9 – 3.9	3.9 – 3.9	3.9 – 3.9	3.9 – 3.9	3.9 – 3.9	4.4 – 4.4	4.4 – 4.4	4.4 – 7.2
V <sub>T</sub> (mL)								
Mean ± SD	344 ± 2	358 ± 22	346 ± 11	369 ± 55	<b>305 ± 10</b>	<b>388 ± 73*</b>	339 ± 7	466 ± 247
First cycle – Last cycle	344 – 342	393 – 345	343 – 373	482 – 338	294 – 320	520 – 343	350 – 331	765 – 310

Abbreviations: PS, pressure support; EPAP, expiratory positive airway pressure; V<sub>T</sub>, tidal volume.

\* *P* < .05 compared to *pre-*event value.

† Even though the statistical analysis did not capture significant difference from *pre-* to *post-*event, the response of the device during the event was considered appropriate.

**Table 3. Event detection and appropriateness of devices' response to the simulated respiratory events**

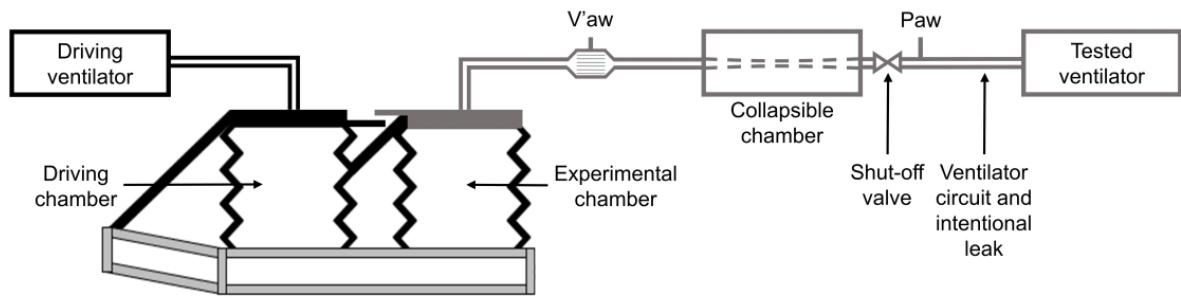
	Vivo 45	Prisma VENT40	BiPAP A40 Pro	Stellar 150
<b>Central Hypopnea</b>				
<i>Detected</i>	Yes	Yes	Yes	Yes
Auto-adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	No	No
<i>Appropriate response</i>	Acceptable	Yes	Acceptable	Yes
Concerns	- $V_T$ overshoot at first post-event cycle	-	- Last event cycle: $V_T = 79\%$ of target $V_T$	-
<b>Central Apnea</b>				
<i>Detected</i>	Yes	Yes	Yes	Yes
Auto-adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	Yes (H)	Yes (H)
<i>Appropriate response</i>	No	Yes	Acceptable	Acceptable
Concerns	- Last event cycle: $V_T = 58\%$ of target $V_T$ - $\uparrow$ EPAP post-event - $V_T$ overshoot at last post-event cycle	-	- Last event cycle: $V_T = 56\%$ of target $V_T$	- $V_T$ overshoot at first post-event cycle
<b>Obstructive Hypopnea</b>				
<i>Detected</i>	Yes	Yes	Yes	Yes
Auto-adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	No	Yes (H)
<i>Appropriate response</i>	Acceptable	No	No	Acceptable
Concerns	- Last event cycle: $V_T = 48\%$ of target $V_T$ - Asynchronies with backup RR activation	- No EPAP modification - $V_T$ overshoot at first post-event cycle	- No EPAP modification - Last event cycle: $V_T = 43\%$ of target $V_T$	- Last event cycle: $V_T = 65\%$ of target $V_T$ - $V_T$ overshoot at first post-event cycle
<b>Obstructive Apnea</b>				
<i>Detected</i>	Yes	Yes	Yes	Yes
Auto-adjustment	Yes	Yes	No	Yes
Scoring	No	Yes (OA)	Yes (OA)	Yes (OA)
<i>Appropriate response</i>	Acceptable	Yes	No	Acceptable
Concerns	- $\uparrow$ PS during the event	-	- No EPAP modification	- $\uparrow$ PS during the event - $V_T$ overshoot at first post-event cycle

**Abbreviations:**  $V_T$ , tidal volume; PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate; H, hypopnea; OA, obstructive apnea.

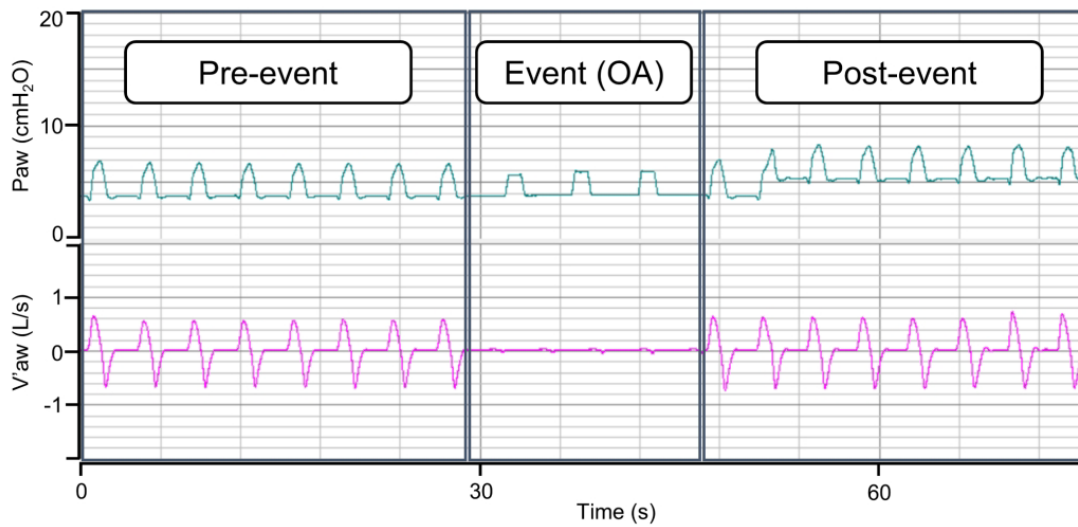
Device response was considered appropriate (“Yes” or “Acceptable”) if the CH was associated with an increase in PS during the event, if the CA was associated with an increase in PS as well as activation of the backup RR during the event, if the OH was associated with an increase in EPAP (and an increase in PS if actual  $V_T$  was below the target  $V_T$ ) either during the event or from *pre-* to *post-*event, and if OA was associated with an increase in EPAP from *pre-* to *post-*event.

The response was considered “acceptable” when the behavior of the device, despite an appropriate response, raised some relevant concerns.

Regarding PS adaptation, concerns were identified if, during an event, the device did not sustain  $V_T$  within [80–120]% of the target  $V_T$  for the last cycle of the event (CH, CA, and OH), or did not reach [80–120]% of mean *pre-*event  $V_T$  after the event (for all events), or induced  $V_T$  overshoot, defined as a difference >20% from mean *pre-*event  $V_T$ .

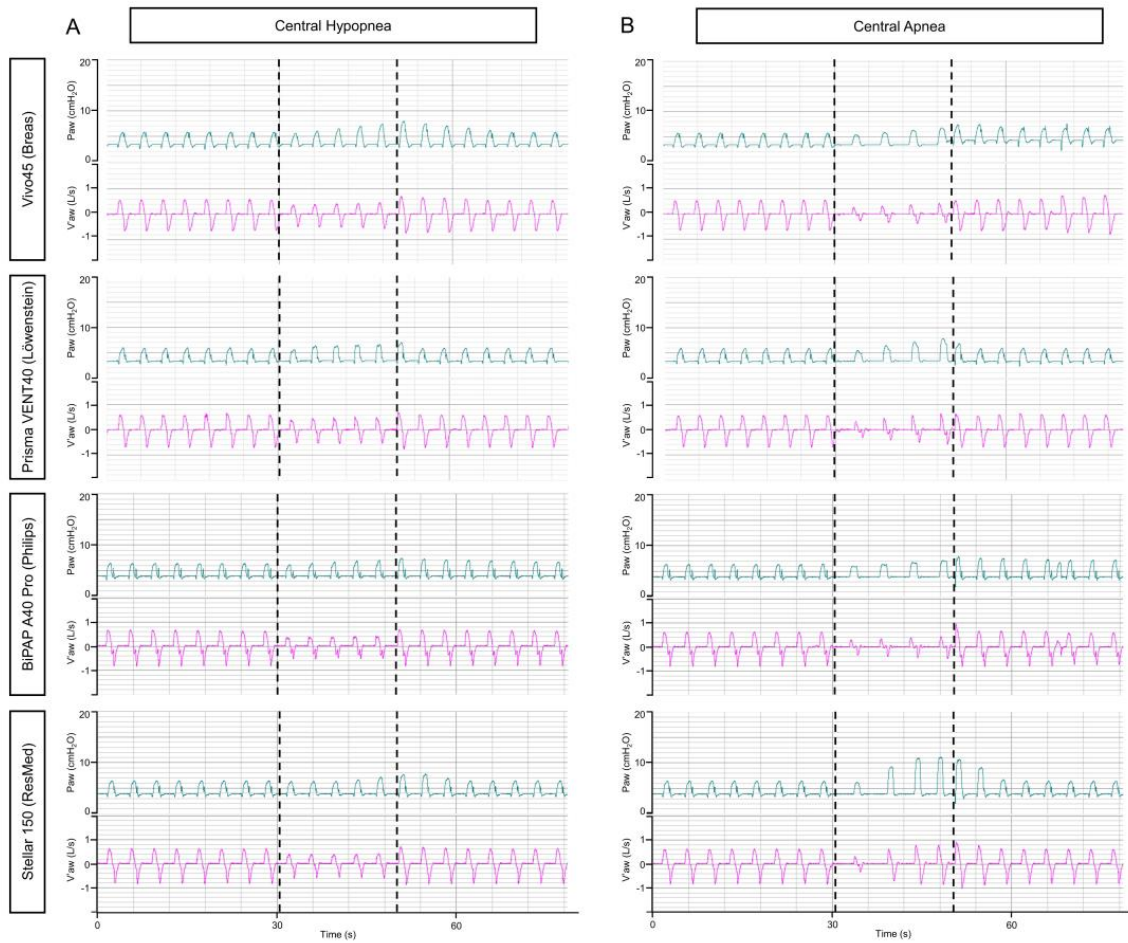


**Figure 1.** Experimental setup.



**Figure 2.** Data acquisition and periods of interest.

Example of data recorded during a simulated episode of obstructive apnea. The periods of interest were the 30 seconds preceding the event (*pre-event* period), 15–20 seconds of event duration (*event* period), and 30 seconds following the event (*post-event* period).  
V'aw, respiratory flow; Paw, airway pressure; OA, obstructive apnea.



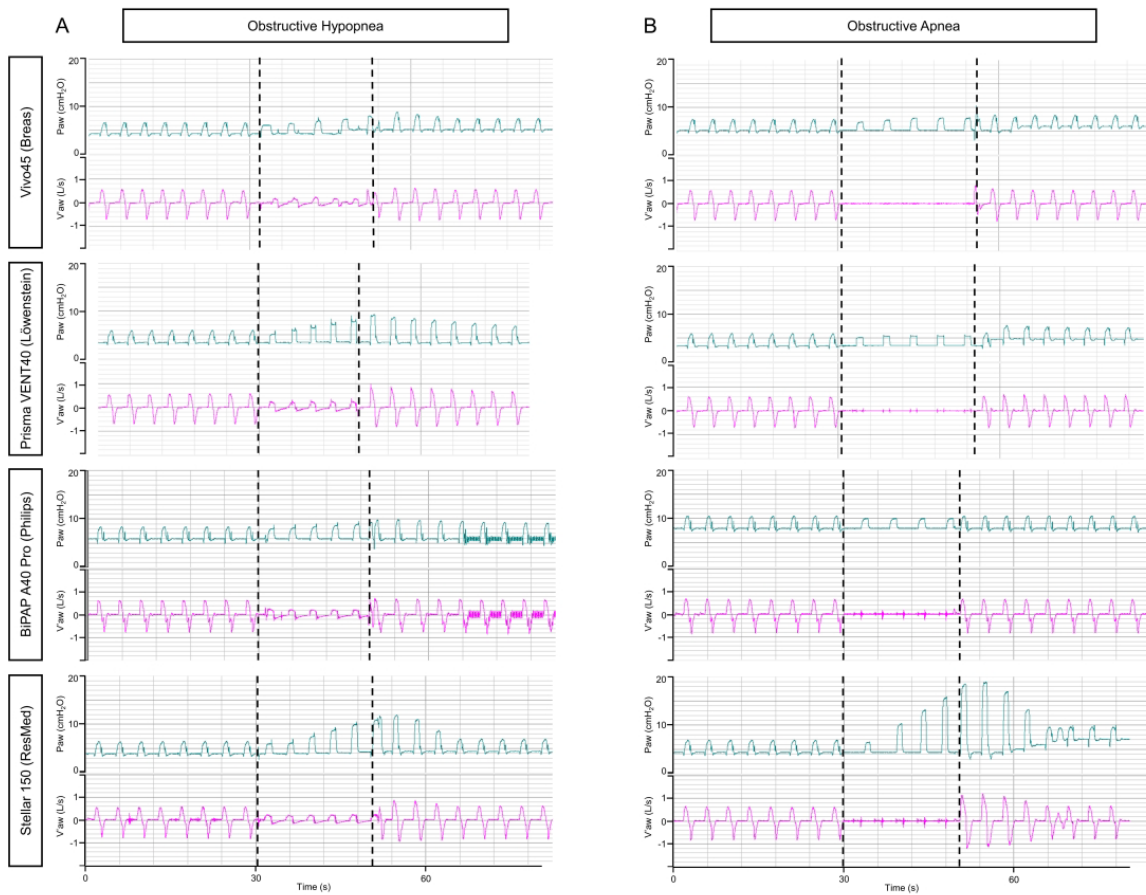
**Figure 3.** Device responses to central hypopnea and apnea.

3A: Central hypopnea

3B: Central apnea.

The dashed vertical lines show the beginning and end of the event period.

V'aw, respiratory flow; Paw, airway pressure.



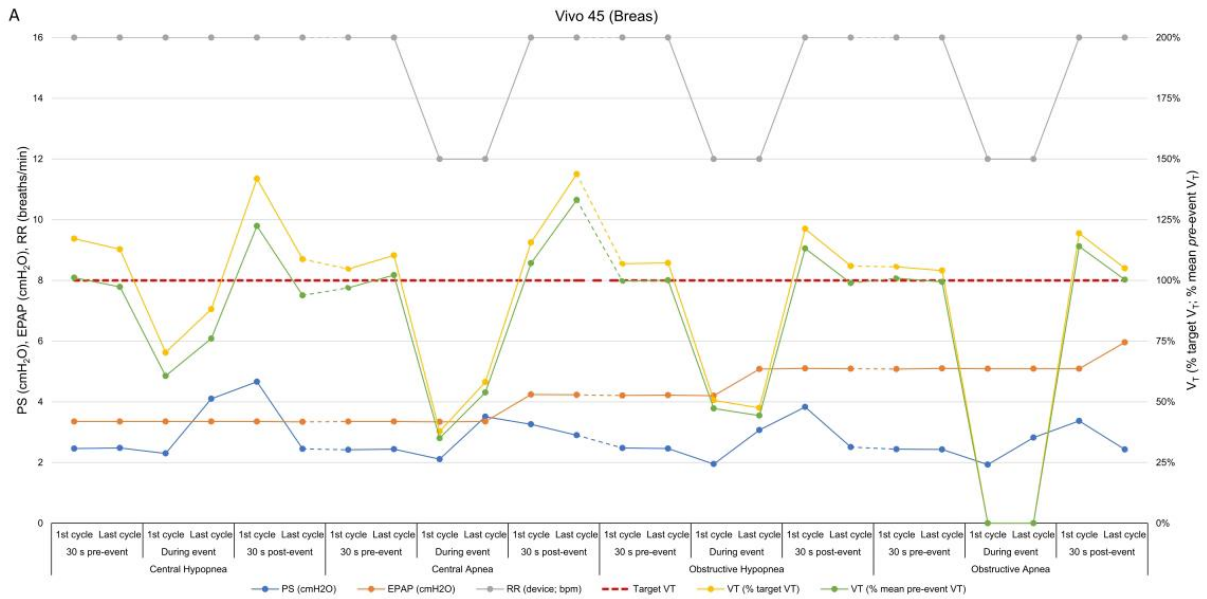
**Figure 4.** Device responses to obstructive hypopnea and apnea.

4A: Obstructive hypopnea

4B: Obstructive apnea.

The dashed vertical lines show the beginning and end of the event period.

V'aw, respiratory flow; Paw, airway pressure.



**Figure 5.** Diagram of dynamic device behavior from the first to the last cycle of each period of interest.

Figure 5A: Vivo45 (Breas)

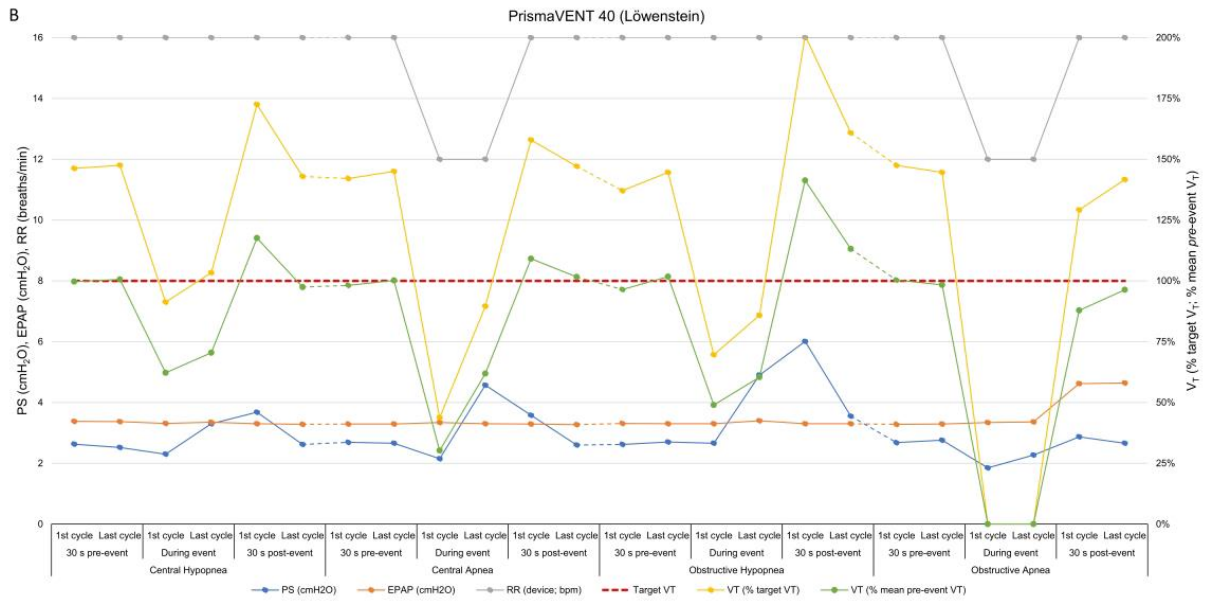
Figure 5B: Prisma VENT40 (Löwenstein)

Figure 5C: BiPAP A40 Pro (Philips)

Figure 5D: Stellar 150 (ResMed)

\*: VT = 294% of target VT; 226% of mean pre-event VT

PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate; VT, tidal volume.



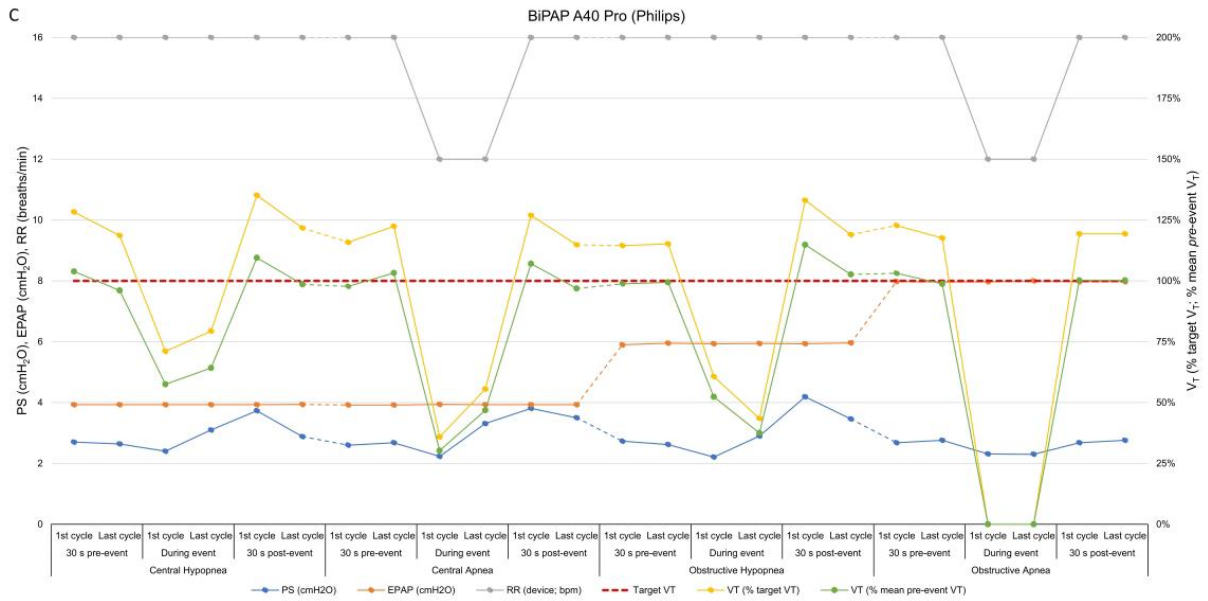
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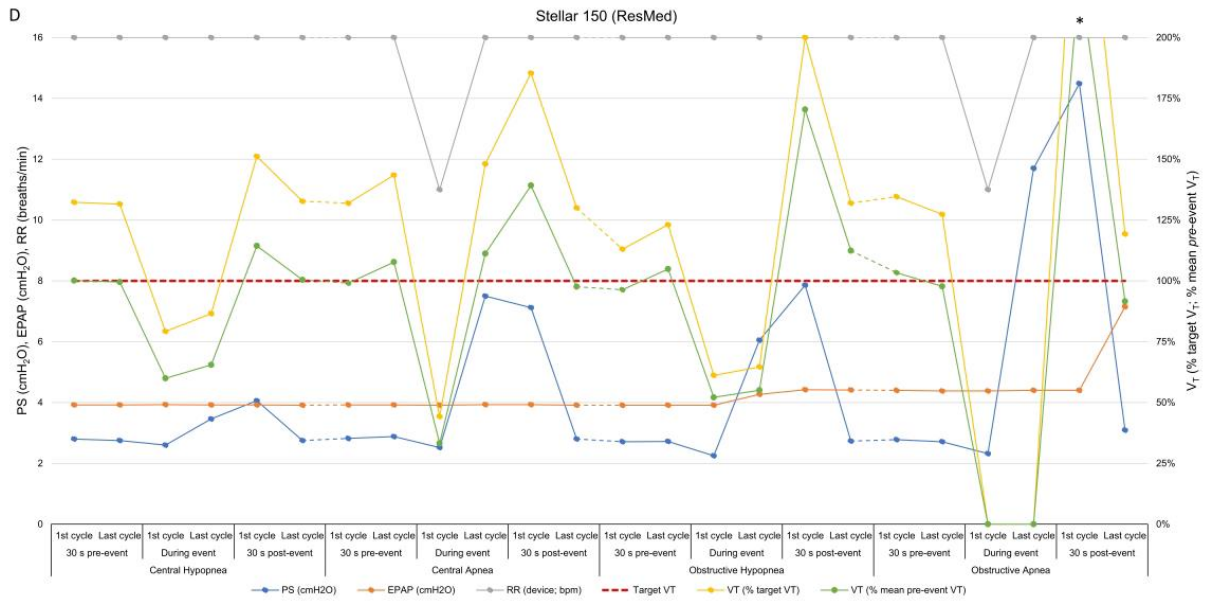


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Figure 5C: BiPAP A40 Pro (Philips)

Figure 5D: Stellar 150 (ResMed)

\*: VT = 294% of target VT; 226% of mean pre-event VT

PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate; VT, tidal volume.

## SUPPLEMENTARY MATERIAL

### **Noninvasive ventilation automated technologies: a bench evaluation of devices' response to sleep-related respiratory events.**

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## SUPPLEMENTARY METHODS

### *Bench model*

The driving ventilator was an Elisee 150 (ResMed Ltd, Bella Vista, NSW, Australia) and was set in pressure-controlled mode with inspiratory pressure 10 cmH<sub>2</sub>O (added to PEEP); respiratory rate (RR) 16 breaths/min; inspiratory time (Ti) 1.2 sec (I:E ratio 1:2). PEEP in the driving chamber was set at 5 cmH<sub>2</sub>O and was adjusted when needed in order to prevent chambers separation at end-expiration.

During inspiration and depending on the tested ventilator pressurization intensity, the experimental chamber could independently rise above the driving chamber. Therefore, at the beginning of inspiration (while both chambers were connected to each other), the flow and volume

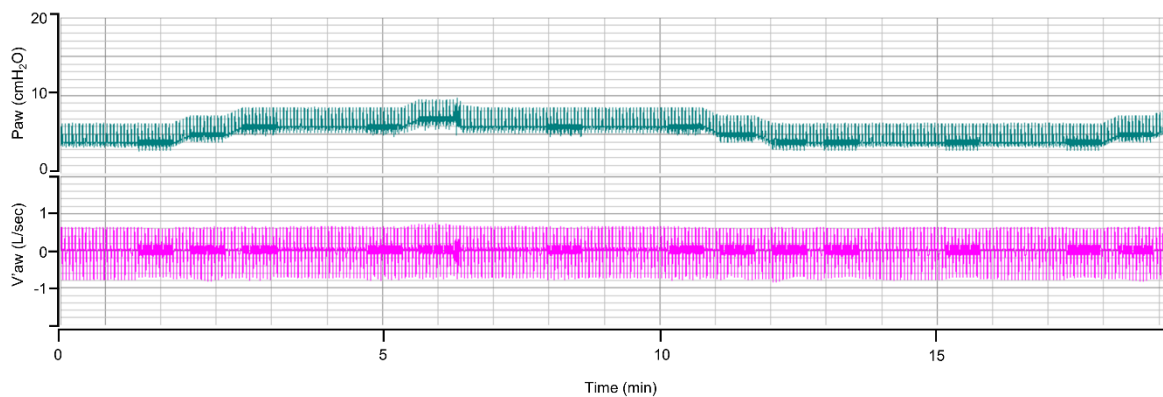
measured in the experimental chamber depended both on the simulated effort and the tested ventilator output. During the second part of inspiration, the tidal volume generated only resulted from the tested ventilator output, accordingly with inspiratory muscle relaxation which may occur before the end of insufflation.<sup>1</sup>

## SUPPLEMENTARY FIGURES

Supplementary Figure 1. Illustration of Philips – BiPAP A40 Pro behavior in the absence of any simulated event.

V<sub>aw</sub>, respiratory flow; P<sub>aw</sub>, airway pressure.

According to its algorithm, BiPAP A40 Pro adjusted EPAP independently from the occurrence of any simulated event. Pressure oscillations are periodically generated by the device in order to assess the resulting amplitude of flow variations. This algorithm allows for identifying the conductance of the system as a surrogate of airway resistance. The device automatically increases EPAP up to a level at which there is no further reduction in the system's resistance. From this level, step by step reduction of EPAP is generated and so on.



Supplementary Figure 2. Schematic presentation of the dynamic behavior of devices from the first to the last cycle of each period of interest – Simulation of the events over a 1-minute duration.

PS, pressure support; EPAP, expiratory positive airway pressure; RR, respiratory rate;  $V_T$ , tidal volume.

Figure 2A: Breas – Vivo45

Figure 2B: Löwenstein – Prisma VENT40

\*:  $V_T = 276\%$  of target  $V_T$

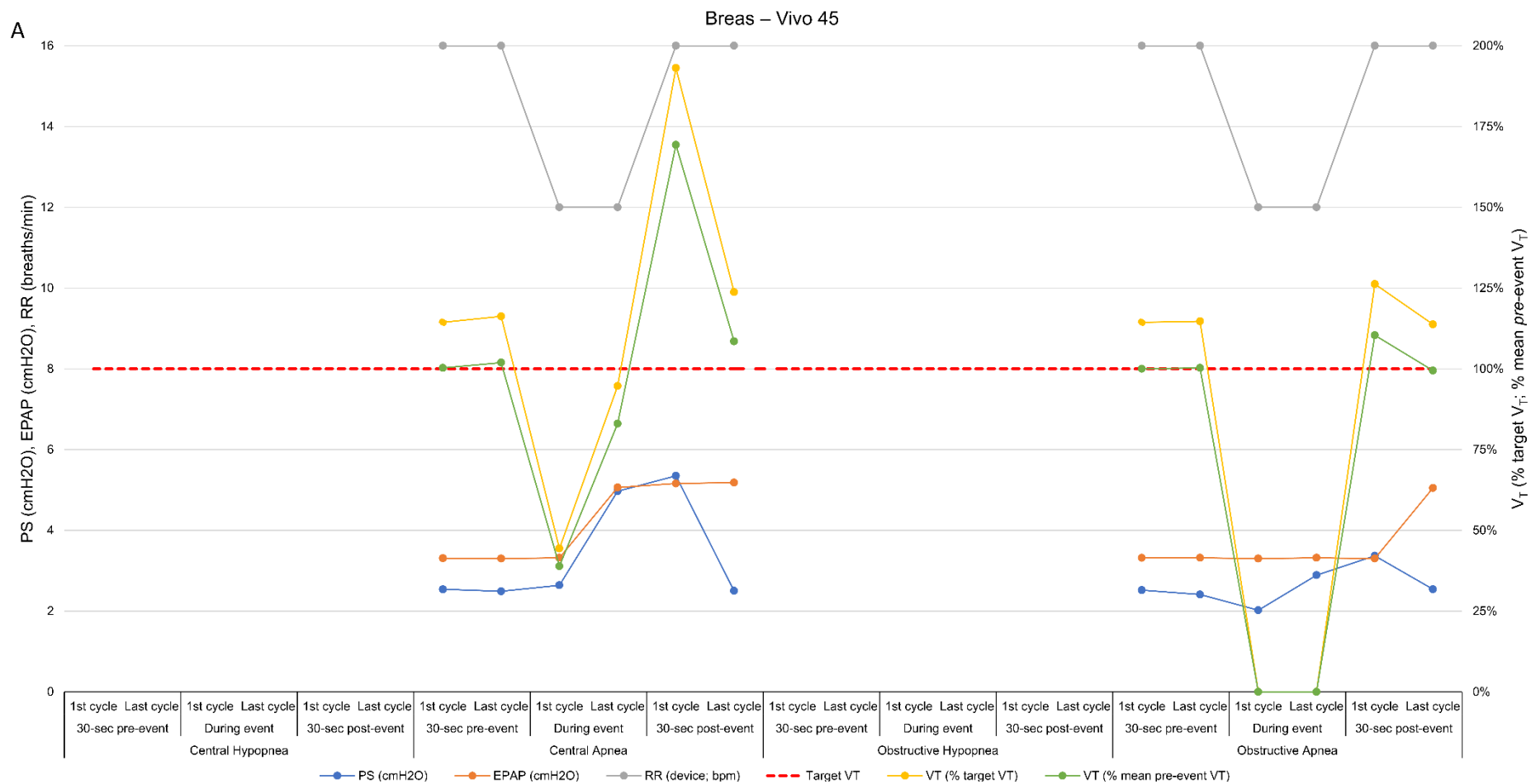
Figure 2C: Philips – BiPAP A40 Pro

\* Note that the greater EPAP level at the beginning of the CA simulation was not induced by the event, but was related to the algorithm of the device as described in supplementary Figure 1.

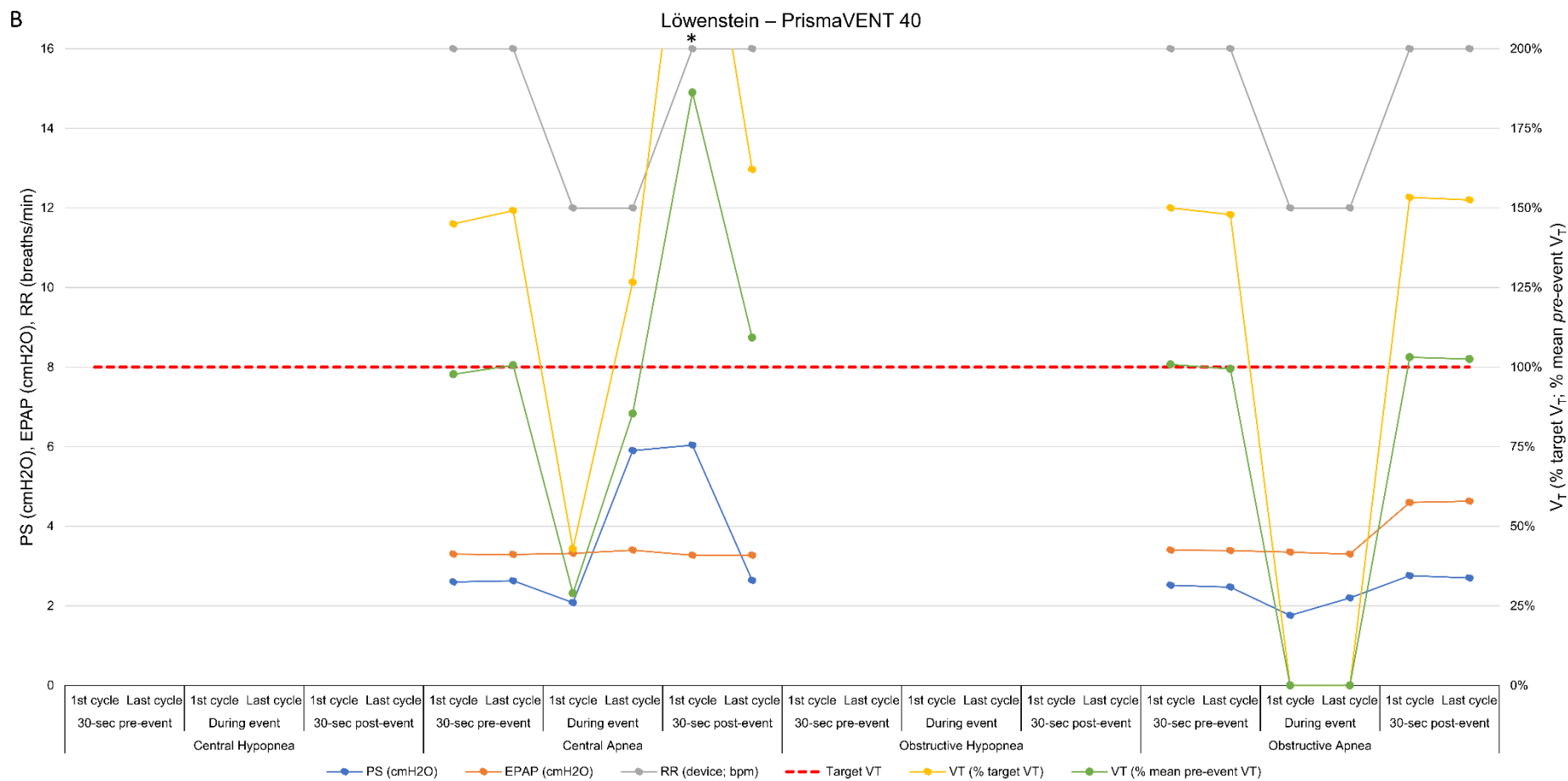
Figure 2D: ResMed – Stellar 150

\*:  $V_T = 255\%$  of target  $V_T$ ;  $231\%$  of mean *pre-event*  $V_T$

Supplementary Figure 2A

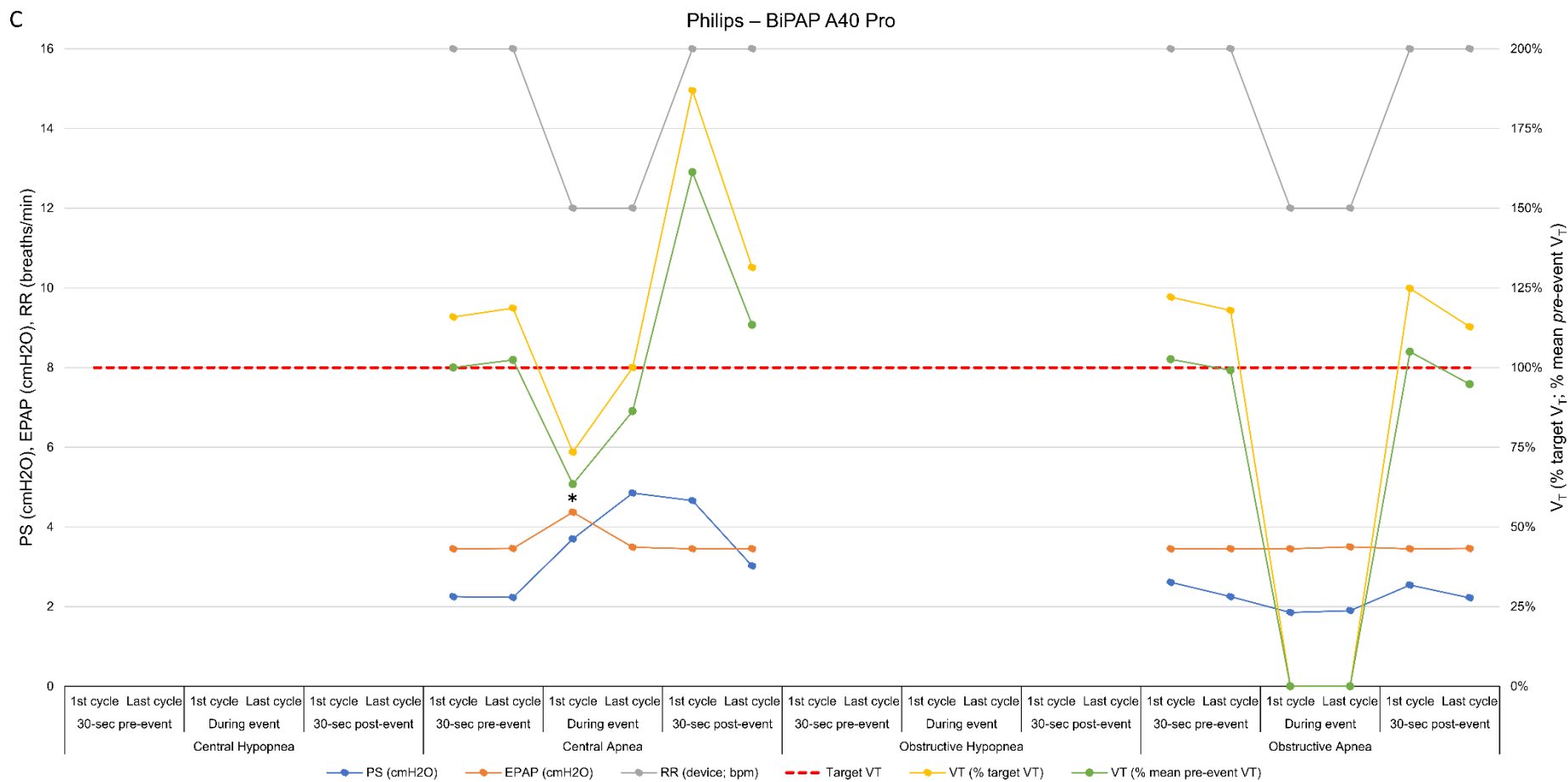


Supplementary Figure 2B

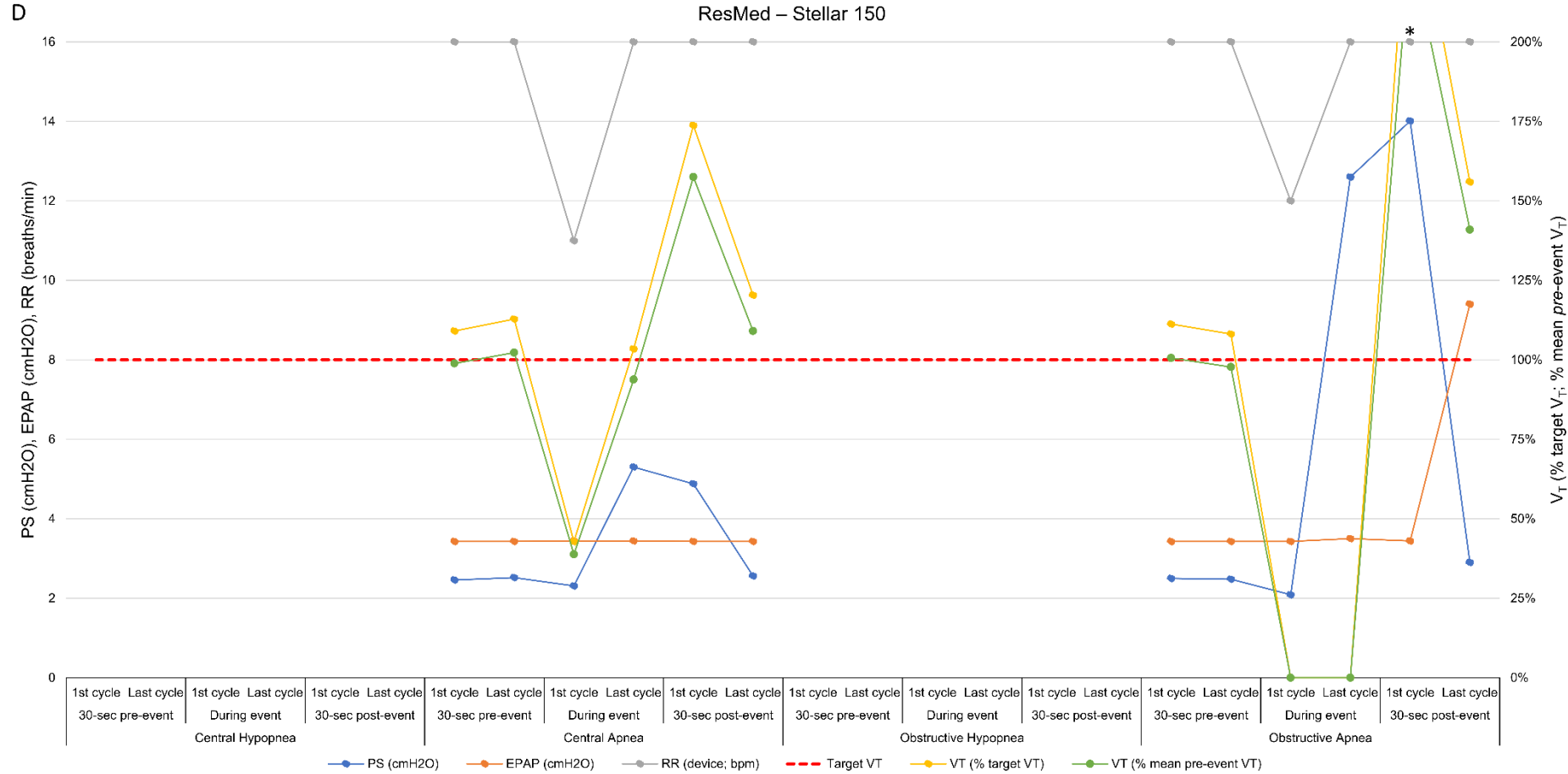




Supplementary Figure 2C



Supplementary Figure 2D



## **SUPPLEMENTARY REFERENCES**

1. Prinianakis G, Plataki M, Kondili E, Klimathianaki M, Vaporidi K, Georgopoulos D. Effects of relaxation of inspiratory muscles on ventilator pressure during pressure support. *Intensive Care Med.* 2008;34:70-74.