Table S3 How to set a ventilator in a Va assured pressure controlled mode (iVAPS)

1. Set the ventilator in iVAPS Mode or iVAPS AE (autoEPAP)
2. Set the target Va value: • The anatomical dead space needs to be calculated in order to estimate the Va. Introduce the patient's height in the ventilator´s calculator. The estimated Va will be displayed.
3. Back-up rate : • In iVAPS the back-up rate - labeled as intelligent back-up respiratory rate (iBR) – uses the patient´s spontaneous respiratory rate as its target rate. It remains untriggered until the patient´s breath rate is below two-thirds of the target patient rate. For example, if patient´s spontaneous respiratory rate is 20/min, the iBR is 14/min. This means that the ventilator starts to deliver mandatory breaths only when the patient's respiratory rate falls below 14/min. Note: in Stellar 150 ventilator (® ResMed, Australia) Target Va and back-up respiratory rate can be also set according to the automatic titration program (´Learn targets´). In this procedure the Va and respiratory rate are automatically estimated by the ventilator. For this purposes, the patient breaths quietly with the mask on under 4 cmH_2O of CPAP over a 20-min period. Once the estimations are displayed, the clinician can resume the final ventilator settings.
4. Set the IPAP limits (the inspiratory pressure support will be constrained between two pressures) • PS minimum: the lowest PS level that the patient should receive to maintain the set Va. The PS value is always above EPAP (i.e. PS 4 cmH2O and EPAP 3 cmH_2O means 7 cmH_2O of inspiratory pressure). • PS maximum: the highest pressure the patient should need to maintain Va in challenging conditions like deep sleep stages and supine body position. Factors such as the patient´s pathology and ventilation tolerance, as well as mask seal should be taken into account.
5. Set the EPAP (baseline pressure) • A minimum per default level of EPAP is always present when using intentional leak

	configuration. iVAPS mode can be only applied with a vented leak configuration system. Set an appropriate EPAP level according to the patient's underlying disease and optimally after a sleep study. Alternatively, $iVAPS_{autoEPAP}$ offers an automatically adjustable EPAP feature. Hereby a minimal and maximal EPAP level must be set.
6.	Set the PS rise time: • Adjust rise time - namely the time the ventilator takes to reach the set inspiratory pressure – based on patient's underlying pathology and comfort. Also take into account the minimum inspiratory time (Timin), i.e. the rise time cannot exceed two-thirds of Timin (see below). • iVAPS also allows to set a so called "fall time" (only Stellar 150 ®). This corresponds to the time the ventilator takes from the end of inspiration to the baseline variable (EPAP). There are no data on clinical impact of this setting.
7.	Set minimum and maximum inspiratory time (Timin and Timax): • During iVAPS, the percentage of inspiratory flow threshold is always the first cycling criteria. Set Timin and Timax according to patient's pathology and the patient´s respiratory rate. • Timax: is the maximum inspiratory time that the patient can reach. Time cycling at the preset Timax will be triggered only when the threshold in inspiratory flow decay percentage is not reached. • Timin: is the minimum allowed inspiratory time. Timin cycling is reached in case of a premature flow cycled breath.

iVAPS, intelligent Volume Assured Pressure Support- ResMed®, Australia; Va, alveolar ventilation; IBW, ideal body weight, formula according to National Institute of Health; CPAP, continuous positive airway pressure; IPAP, inspiratory positive airway pressure; PS, pressure support; EPAP, expiratory positive airway pressure

Va target setting

iVAPS (intelligent Volume Assured Pressure Support- ResMed®, Australia) is designed to maintain a preset target alveolar minute ventilation by monitoring delivered ventilation, adjusting the pressure support and providing an intelligent backup breath (iBR) automatically.

Alveolar ventilation (Va) means to consider only the fresh alveolar gas or effective Vt ($Vt_{effective}$) that is actively participating in the gas exchange. Therefore, of every inspiration, the amount of gas left behind at the anatomical dead space must be substracted ($Vt - Vd = Vt_{eff}$). Since an accurate Va measurement would be too cumbersome, iVAPS proposes to estimate the VA based on expiratory volume (VE) minus an estimation of Vd (based on anthropometric data).

Knowledge of the size of the dead space is important for proper mechanical ventilation. Some advocate that dead space can be predicted using a relationship of 2.2 milliliter per kg of body weight.[1] However, in 1955 Radford showed that anatomic dead space is roughly correlated with body weight.[2] This poor correlation contradicts the suggestion that dead space can be estimated from body weight.

A further caveat must be considered. Although in healthy lungs the alveolar dead space is small (156 ± 28 mL or 26% of Vt),[3] this value is significantly increased in COPD patients and interstitial lung diseases.

The second bias in iVAPS system is that Vtexp is just an estimation and not a measurement of the real value. This matter - shared by the majority of VAP ventilators- was extensively discussed in the main text.

References

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3. Fowler W.S. (1948). "Lung Function studies. II. The respiratory dead space". Am. J. Physiol. 154: 405–416.