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REVIEW

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# Automating the weaning process with advanced closed-loop systems

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**Abstract** *Background:* Limiting the duration of invasive ventilation is an important goal in caring for critically ill patients. Several clinical trials have shown that compared to traditional care, protocols can reduce the total duration of mechanical ventilation. Computerized or automated weaning has the potential to improve weaning, while decreasing associated workload, and to transfer best evidence into clinical practice by integrating closed-loop technology into protocols that can be operationalized continuously. *Discussion:* In this article, we review the principles of automated systems, discuss automated systems that can be used during weaning, and examine the best-current evidence from randomized trials and observational studies supporting their use. We highlight three commercially available systems (Mandatory Minute Ventilation, Adaptive Support Ventilation and SmartCare™) that can be used to automate the weaning process. We note advantages and disadvantages associated with individual weaning systems and differences among them. *Conclusions:* We discuss the potential role for automation in complimenting clinical acumen, reducing practice pattern variation and facilitating knowledge translation into clinical practice, and underscore the need for additional high quality investigations to evaluate automated weaning systems in different practice settings and diverse patient populations.

## Introduction

Weaning is the process during which mechanical ventilation is gradually or abruptly withdrawn. It is also the time during which the work of breathing is transferred from the ventilator back to the patient. Weaning is a multifaceted process which has traditionally required clinicians to assimilate objective measurements and subjective assessments into clinical decisions regarding the timing and methods used to liberate patients from invasive ventilation. Weaning accounts for approximately 40% of the total time spent on mechanical ventilation [1, 2]. While effective, invasive ventilation is associated with the development of various complications [3] and has been demonstrated to be a key factor contributing to intensive care unit (ICU) costs [4]. For these reasons,

minimizing the duration of invasive ventilation is an important consideration in the management of critically ill patients requiring invasive ventilation [5].

Over the past decade, scientific investigations have focused on strategies to limit the duration of ventilation through early identification of weaning candidates [6–8], the conduct of spontaneous breathing trials (SBTs) [9–11] and strategies to reduce support in patients who fail a SBT [12–14]. Several modes and techniques can be used to facilitate weaning. The optimal strategy to wean patients from invasive ventilation remains to be elucidated. Compared to traditional care, several randomized controlled trials (RCTs) have shown that protocols can reduce the total duration of mechanical ventilation and the time to mechanical ventilation discontinuation [6–8]. Notwithstanding, studies in selected patient populations [15, 16] or unique environments [17] have not consistently demonstrated a beneficial effect of protocol-directed weaning compared to conventional weaning. Moreover, despite large-scale implementation, many barriers exist to implementing weaning protocols in clinical practice [18, 19]. In this regard, computerized (or automated) weaning may not only facilitate weaning but also translation of best evidence into clinical practice by integrating closed-loop technology into protocols that can be operationalized continuously. In this review, we discuss the principles of automation and review the evidence supporting use of advanced closed-loop systems to facilitate weaning critically ill patients from invasive ventilation.

## Principles of automated systems

Classically, the ventilator support delivered to critically ill patients is determined by clinicians who manually adjust ventilator settings. Newer ventilators use principles of closed-loop control [20] to perform basic operations such as generating inspiratory pressure and, inspiratory flow, as well as, more sophisticated functions such as attaining set tidal volume by breath-to-breath regulation of inspiratory pressure (dual-control modes). These ventilators may also offer modes or strategies that integrate patient response into ventilator management using more advanced closed-loop systems. With advanced closed-loop control, selected parameters are measured and ventilator support is adapted to meet individual patient needs [21]. By enabling *interaction* between patients and ventilators, newer closed-loop systems are expected to improve tolerance of mechanical ventilation, reduce work of breathing and enhance patient-ventilator synchrony.

Closed-loop systems modify ventilator parameters by operationalizing predetermined algorithms and adapting ventilator output by comparing measured (actual) values of specific parameters to target (ideal) values. Closed-loop systems minimize or equilibrate (negative feedback) or amplify (positive feedback) differences between measured and target values. With closed-loop systems ventilator control is executed at specific times such as after fixed or predetermined time intervals, or during the next ventilator cycle. Newer closed-loop systems can adapt ventilator support in patients who are dependent on mandatory breaths, transition patients from controlled modes to support modes and automate the weaning process. In this review, we highlight three commercially available systems that can be used in weaning critically ill patients from invasive ventilation including mandatory minute ventilation (MMV) (Evita 4, Draeger Medical Inc, Luebeck, Germany), adaptive support ventilation (ASV) (Galileo, Raphael and Hamilton—G5, Hamilton Medical AG, Rhaezuens, Switzerland), and SmartCare™ (Draeger Medical Inc, Luebeck, Germany). We focus on MMV

**Table 1** Comparison of closed-loop systems

| Automated system feature | MMV | ASV | SmartCare™ |
|---|---|---|---|
| Breath support | VC, dual control SIMV + PS | Dual control SIMV + dual control PS | PS |
| Operating principle | Mandatory frequency to achieve user set minute ventilation | Automatic targets for $V_T$ and RR to achieve user set minute ventilation, mandatory frequency to achieve RR target, PC or PS to achieve $V_T$ target | PS adapted to maintain in respiratory comfort zone |
| Breath type | Mandatory and spontaneous | Mandatory and spontaneous | Spontaneous only |
| Clinician control | $V_T$, Insp time, RR | Minute ventilation | No |
| Frequency of determination/ adaptation | 7.5 s | Breath-to-breath | 2–5 min |
| Automated SBTs | No | No | Yes |

*MMV* Mandatory minute ventilation (Draeger Medical Inc, Luebeck Germany), *ASV* adaptive support ventilation, *VC* volume control, *PC* pressure control, *SIMV* synchronized intermittent mandatory ventilation, *PS* pressure support, *Insp Press* inspiratory pressure, *RR* respiratory rate, *WOB* work of breathing, *Vt* tidal volume, *Insp time* inspiratory time

available on the Evita 4 ventilator (Draeger Medical Inc, Luebeck, Germany) since MMV on the Veolar (Hamilton Medical AG, Rhaezuens, Switzerland) and CPU-1 Intensive Care (Ohmeda Medical, Columbia, MD, USA) ventilators are not currently marketed. In Table 1, we highlight the characteristics of each of the aforementioned systems.

## Automated weaning strategies and modes

### Mandatory minute ventilation

MMV was first described by Hewlett and colleagues in 1977 to improve weaning [22]. This early version of MMV was based on mechanical closed-loop control as opposed to the electronic automation of mandatory breaths used subsequently in the CPU-1 Intensive Care ventilator (Ohmeda Medical) and in more recent versions of MMV. MMV is expressed as different ventilation modes on different ventilators. MMV on the Evita 4 ventilator (Draeger Medical Inc, Luebeck, Germany), CPU-1 Intensive Care ventilator (Ohmeda Medical) and Sechrist IV-100B (Sechrist Industries Inc, Anaheim, CA, USA) is based on closed-loop control of mandatory rate with user-set mandatory breaths, tidal volume and user-set pressure support (PS) for spontaneous breaths. This differs from MMV on the Hamilton Veolar ventilator (Hamilton Medical AG, Rhaezuens, Switzerland) which automatically adjusts the level of PS provided in accordance with user-set minute ventilation.

MMV (Draeger Medical Inc, Luebeck Germany) combines features of controlled ventilation with mandatory breaths and pressure support ventilation to augment spontaneous respiratory efforts. MMV, on this ventilator, can provide breaths in several modes including volume control (VC) or synchronized intermittent mandatory ventilation (SIMV) with PS [23] and can therefore be used in patients requiring mandatory breaths and in spontaneously breathing patients. With MMV, clinicians set tidal volume ($V_T$) and a mandatory breath rate thereby defining a target minute ventilation. The ventilator adapts the mandatory breath rate to meet the predetermined minute ventilation by taking the patient's spontaneous respiratory rate (RR) into consideration. Unlike, SIMV which delivers a constant preset mandatory rate, the mandatory rate is variable with MMV. If a patient's spontaneous breathing meets or exceeds the preset minute volume, no mandatory breaths are provided in MMV. Conversely, if the patient's minute volume falls below the preset minute ventilation, mandatory breaths will be delivered at a fixed rate in MMV mode to ensure the desired minute ventilation is achieved. With Draeger MMV, the level of PS provided is not adjusted by the ventilator [23].

### Weaning with MMV

Few clinical investigations have been conducted comparing MMV to alternate modes of ventilation or modes of ventilation used in weaning with most investigations conducted in the neonatal population. Davis and colleagues [24] conducted the only published weaning RCT involving MMV (CPU-1Intensive Care Ventilator, Ohmeda Medical, Columbia MD) in adults. In this study, the authors randomized 22 patients to MMV and 18 patients to IMV weaning. The authors found that compared to IMV, MMV significantly reduced weaning time (33.3 vs. 4.8 h; $P = 0.0005$), successfully weaned a similar proportion of patients at 4-h following extubation (86 vs. 89%) and was less cumbersome for ICU staff to manage [24]. In a cross-over study of 15 very low birth weight infants, Claure and co-workers found that compared to IMV, MMV (Sechrist IV-100B; Sechrist Industries Inc, Anaheim, CA, USA) reduced $V_T$ and airway pressures while significantly reducing the number of mandatory breaths ($15 \pm 2.8$ vs. $8.6 \pm 2.9$ breaths/min; $P < 0.001$) delivered [25]. These findings were supported by a cross-over study conducted by Guthrie and colleagues that compared MMV (Evita 4; Draeger Medical Inc, Luebeck, Germany) to SIMV applied in random order for 2-h each in 20 neonates. Compared to SIMV, the authors showed that MMV significantly reduced mean airway pressures, increased spontaneous respirations and reduced the number of mandatory breaths delivered [26].

### Adaptive support ventilation

Adaptive support ventilation was initially introduced as adaptive lung ventilation by Laubscher in 1994 [27, 28]. ASV was designed to achieve a desired minute ventilation by providing the optimal combination of $V_T$ and RR, determined by Otis' equation [29], for individual patients. Otis' equation calculates an *ideal* RR (associated with the least energy expenditure) by considering the patient's dead space, minute ventilation and the expiratory time constant of their respiratory system [30]. The ASV algorithm uses ideal body weight to calculate the patient's theoretical dead space volume (2.2 m/s/kg) and "normal" minute ventilation (100 m/s/kg $min^{-1}$). Clinicians can increase or decrease the calculated minute ventilation by targeting a percentage of the normal minute ventilation based upon clinical assessment of individual patients. *Ideal* $V_T$, in turn, is obtained by dividing minute ventilation by the *ideal* RR calculated by Otis' equation. Similar to pressure control (PC) ventilation, ASV adjusts inspiratory pressure to reach the target inspired $V_T$. *Actual* RR, $V_T$ and respiratory mechanics are measured on a breath-to-breath basis and ideal RR and inspiratory pressure are reassessed using Otis' equation. Ideal and actual RR and $V_T$ are indicated on the ventilator display.

When spontaneous respiratory efforts are detected, the ASV algorithm switches from PC to PS ventilation and continues to monitor patient $V_T$ and RR. ASV titrates inspiratory pressure to achieve the calculated $V_T$, as long as the patient's RR meets or exceeds the ideal RR. In the event that the patient's RR decreases below the ideal threshold, the ASV algorithm adds mandatory breaths to meet the target (ideal) RR. The strategic rules of ASV focus on maintaining appropriate ventilation by adapting the ventilatory pattern to passive mechanics, maintaining adequate carbon dioxide elimination, providing control in the setting of absent or insufficient drive and guarding against dynamic hyperinflation. Thus, ASV can provide support to patients who require controlled or assisted ventilation and can be used to facilitate weaning.

## Weaning with ASV

In stable patients capable of initiating spontaneous breaths, the ASV algorithm will progressively and automatically reduce inspiratory pressure as the patient's respiratory mechanics improve. Weaning is completed when all breaths are spontaneous and patients demonstrate adequate and stable gas exchange for a few hours at low inspiratory pressure (e.g., <8 cm $H_2O$).

Preliminary studies in adults suggest that ASV can simplify ventilator management and reduce the time to extubation in predominantly postoperative patient populations. Two RCTs conducted by Sulzer and coworkers [31] and Petter and colleagues [32], involving 49 and 34 post-cardiac surgery patients, respectively, found that compared to protocols using SIMV and PS, ASV resulted in fewer changes in the ventilator settings [31, 32]. Additionally, Petter and colleagues noted that ASV resulted in significantly fewer high-inspiratory pressure alarms and fewer interventions to modify ventilator settings from the ICU team providing care [32]. Sulzer and colleagues also noted that ASV significant reduced the duration of endotracheal intubation [3.2 (2.5– 4.6) vs. 4.1 (3.1–8.6) h; $P < 0.02$] and resulted in more fast track successes (successful extubations at 6 h) (15/16 vs. 12/20, $P < 0.01$) in a post-hoc analysis [31]. In two cohort studies, Linton and coworkers, reported successful weaning, using an earlier version of ASV, in 21 patients with normal or diseased lungs [33] and in 12/27 chronically ventilated patients successfully weaned over 2 months with ASV [34]. Finally, Cassina et al. reported that 86% of a cohort of 155 patients following cardiac surgery could be successfully extubated using ASV along the continuum of ventilator support [35]. Arnal and colleagues recently published a prospective cohort study of 243 patients invasively ventilated with ASV demonstrating that in passively breathing patients ventilatory parameters ($V_T$ and RR) differed with ASV depending on the patient's respiratory mechanics [for example, chronic obstructive pulmonary disease (COPD) patients had higher $V_T$ and lower RR compared to patients with acute lung injury] [36].

## SmartCare™

SmartCare™, also known as "Neoganesh" or the Automated Weaning System, is the first commercially available automated system specifically designed to guides the weaning process. SmartCare™ continuously enacts a weaning protocol in PS mode based on measurements of RR, $V_T$ and the partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) averaged over 2–5 min. SmartCare™ aims to maintain patients in a "comfort zone" of respiration, by adapting the level of PS provided to spontaneously breathing patients, and automatically initiates a SBT when patients meet predefined criteria.

SmartCare™ was designed for spontaneously breathing, hemodynamically stable patients who are invasively ventilated with stable oxygenation. Separate software guides the weaning process in pediatric (≤35 kg) and adult (35–200 kg) patients. To initiate SmartCare™, the clinician must enter information regarding the patient (weight, presence of COPD and/or a central neurological disorder), airway prosthesis (endotracheal tube or tracheostomy) and type of humidification system [heat and moisture exchanger (HME) or heated humidifier (HH)] in use. While information regarding patient characteristics determines the limits for $V_T$, RR, and $P_{ET}CO_2$, equipment-related information (airway prosthesis and humidification system) governs the level of PS at which a SBT is initiated. If desired, SmartCare™ can be set to suspend weaning at night to allow patients to rest. SmartCare™ is not recommended when neurologic conditions impact on breathing control [37], in over-sedated patients, and patients with severe bronchospasm [38]. Moreover SmartCare™ is not recommended in severely agitated patients, wherein an elevated RR may result in undue increases in the level of PS provided, and in severe polyneuropathy or myopathy as SmartCare PS may overestimate respiratory function in these patients [37].

## Phases of SmartCare™ weaning

The SmartCare™ weaning process involves three distinct phases: adaptation, observation and maintenance.

### *Adaptation*

During adaptation, SmartCare™ strives to maintain patients in a state of respiratory comfort (*normal ventilation*) (see Table 2) by adapting the level of PS provided

based on the individual patient's RR, $V_T$ and the $PETCO_2$. The system measures these parameters on a breath-to-breath basis and computes their average values every 2–5 min. The average values are used to classify the patient's breathing pattern (ventilator diagnosis) based on predetermined thresholds (minimum and maximum RR, minimum $V_T$, and maximum $P_{ET}CO_2$) and adapt the level of PS [above positive end-expiratory pressure (PEEP)] provided accordingly (see Table 2). In SmartCare™, the minimum and maximum RR threshold are set at 15 and 30 breaths/min (alternatively, 34 breaths/min in patients with neurologic disorders) and a lower threshold for $V_T$, based on patient weight, is established (250 ml for patients <55 kg and 300 ml for patients >55 kg). A maximum $P_{ET}CO_2$ threshold of 55 mmHg is used except for patients with COPD in whom a threshold of 65 mmHg is used. Average values of RR, $V_T$ and $P_{ET}CO_2$ falling within these constraints define *normal ventilation*.

When ventilatory parameters fall outside of the predetermined constraints, SmartCare™ adapts the level of PS provided to restore a state of *normal ventilation*. SmartCare™ increases PS in response to *tachypnea, severe tachypnea, hypoventilation* and *insufficient ventilation* and lowers PS in response to a diagnosis of *hyperventilation* (see Table 2). The magnitude of the increments or decrements in PS range from 2 to 4 cm $H_2O$ and are determined by the patient's preceding pattern of breathing. For example if a patient's RR is >30 breaths/min (or >34 breaths/min with neurologic disorders) and $P_{ET}CO_2$ and $V_T$ fall within the accepted ranges, SmartCare™ establishes a diagnosis of *tachypnea* and increases PS by 2 cm $H_2O$. Similarly, if a patient's RR is >36 breaths/min with the same $P_{ET}CO_2$ and $V_T$, SmartCare™ considers the patient to be s*everely tachypneic* and increases PS by 4 cm $H_2O$. Conversely, if the patient's RR falls to <12 breaths/min with acceptable $V_T$ and $P_{ET}CO_2$ a diagnosis of *hyperventilation i*s made and PS is reduced by 4 cm $H_2O$. When $V_T$ or $P_{ET}CO_2$ fall outside the reference ranges, SmartCare™ classifies the patient as having *insufficient ventilation* and increases PS by 2 cm $H_2O$. Once patients can be maintained in a state of *normal ventilation,* SmartCare reduces the level of PS provided by 2–4 cm $H_2O$ at 15, 30 or 60 min intervals depending on the preceding level of PS.

### *Observation*

In addition to adapting and adjusting the level of PS in accordance with the patient's needs, SmartCare™ automatically initiates and conducts SBTs when predefined

**Table 2** Adaptation in SmartCare™

| Ventilator classification | Defining parameters | | | Consequence |
|---|---|---|---|---|
| Normal ventilation | RR | 15–30 b/min | No neuro dx | No immediate modification of the PS level |
| | | 15–34 b/min | Neuro dx | |
| | $V_T$ | >300 ml | >55 kg | Subsequently, will attempt to decrease PS by 2 or 4 cm $H_2O$ at 15, 30, 60 min depending on the current level of PS |
| | | >250 ml | 36–55 kg | |
| | $ETCO_2$ | <55 mmHg | No COPD | |
| | | <65 mmHg | COPD | |
| Insufficient ventilation | Acceptable RR but $V_T$ is too low or $ETCO_2$ is too high | | | Immediately increases PS by 2 or 4 cm $H_2O$ depending on the current PS level |
| Hypoventilation | Low RR acceptable $V_T$ and high $ETCO_2$ | | | Immediately increases PS by 4 cm $H_2O$ |
| Central hypoventilation | Low RR and low $V_T$ and high $ETCO_2$ | | | No modification[a] |
| Tachypnea | High RR acceptable $V_T$ and acceptable $ETCO_2$ | | | Immediately increases PS by 2 or 4 cm $H_2O$ depending on the current PS level[a] |
| Severe tachypnea | Very high RR (>36 b/min) acceptable $V_T$ and acceptable $ETCO_2$ | | | Immediately increases PS by 4 cm $H_2O$[a] |
| Hyperventilation | Low RR acceptable $V_T$ and acceptable $ETCO_2$ | | | Immediately reduces PS by 4 cm $H_2O$ |
| Unexplained hyperventilation | High RR acceptable $V_T$ and low $ETCO_2$ | | | No modification[a] |

*RR* respiratory rate, *$V_T$* tidal volume, *$ETCO_2$* end tidal carbon dioxide, *Neuro* neurologic diagnosis, *COPD* chronic obstructive pulmonary disease, *PS* pressure support

[a] Ventilator alarm sounds with three consecutive classifications. The operator is required to check the patient's condition

thresholds are achieved. The transition to a SBT (or observation period) is not apparent to observers but is displayed on the ventilator. A SBT is initiated once patients achieve a minimum level of PS in a state of *normal ventilation* with PEEP $\leq$ 5 cm $H_2O$. The minimum PS level is determined by the type of airway prosthesis and humidification system in use. PS levels of 5 and 7 cm $H_2O$ are required to initiate a SBT with HH and a tracheostomy tube or endotracheal tube, respectively. With HME, SBTs are initiated at 9 and 12 cm $H_2O$ with a tracheostomy or an endotracheal tube, respectively. Increased PS is provided during SBTs conducted with HME based on evidence from physiologic studies demonstrating that HMEs reduce endotracheal tube patency, increases dead space and work of breathing [39–42]. The duration of a SBT is determined by the patient's preceding pattern of breathing and the level of PS at SmartCare™ initiation. For example, a SBT will be 60 min in duration if the PS level at the beginning of the current session was <20 cm $H_2O$ and 120 min if the initial PS was $\geq$20 cm $H_2O$.

During SBTs, the patient's ventilatory parameters are continuously measured. As long as the patient's breathing pattern remains stable, the PS provided during a SBT remains constant. If a patient requires less support during a SBT (e.g., hyperventilation classification) the level of PS can be decreased to 5 cm $H_2O$. The system will terminate the SBT if the level of PS is increased during a SBT, allowing for up to 2 instabilities (classifications other than *normal ventilation* or *hyperventilation*). If the level of PS later returns to the minimum value necessary to initiate a SBT, a new observation period begins. This cycle can be iterative and terminates when the patient successfully completes an observation period and a message is displayed to *"Consider Separation"* of the patient from the ventilator. The patient may then be extubated if extubation criteria are met.

### *Maintenance*

Following a successful SBT and display of the message to "Consider Separation", SmartCare™ enters the maintenance phase. The message will be displayed as long as the patient remains stable allowing for minor instabilities. If the patient's ventilation becomes unstable (i.e., a diagnosis other than *normal ventilation*), SmartCare™ adapts the assistance provided to restore the patient to a state of *normal ventilation.* SmartCare™ incorporates specific strategies to manage instabilities which depend on the level of PS preceding the instability and the duration of the instability. These strategies are not restricted to the maintenance phase.

The Automated Weaning System has been evaluated in prospective, observational studies and a multicentre RCT. Early physiologic studies demonstrated that SmartCare™ reduced patient work of breathing and respiratory distress [43]. Moreover, with regard to mechanical ventilation discontinuation, SmartCare™ was at least as good as intensivists [44] and, in some cases, recognized patient readiness to undergo a SBT earlier than intensivists [45]. A concealed, RCT conducted in five European centres involving 144 patients, ready to tolerate assisted ventilation in PS mode, demonstrated that compared to physician-directed weaning, SmartCare™ decreased the median duration of ventilation from 4 to 2 days ($P = 0.02$), the total duration of ventilation (9 vs. 6.5 days, $P = 0.03$) and resulted in nonsignificant differences in the proportion of patients requiring reintubation at 72-h (22 vs. 16%, $P = 0.40$) [46]. Compared to physician-directed weaning, the authors noted a significant decrease in median ICU length of stay (15.5 vs. 12.0 days, $P = 0.02$) and a nonsignificant trend toward fewer patients requiring prolonged ventilation (>21 days) (15.7 vs. 6.7%, $P = 0.11$) favoring SmartCare™.

## Differences among automated weaning systems

Unlike MMV and ASV which are new modes of ventilation, SmartCare™ is not a new mode of ventilation, but rather a new strategy based upon an established mode of ventilation, PS [12]. While MMV and ASV can provide support to patients who require mandatory breaths, candidates for SmartCare™ weaning must be able to breathe spontaneously in PS mode. Whereas clinicians control $V_T$, inspiratory time and RR with MMV, ASV is adaptive, endeavoring to select breathing patterns that optimize patient work of breathing. Assessments for mandatory breaths are made in MMV (Draeger Medical Inc, Luebeck, Germany) every 7.5 s. Conversely, adaptations in respiratory pattern are made on a breath-by-breath basis with ASV and at 2–5 min intervals with SmartCare™ (see Table 1). MMV is a more sophisticated system compared to SIMV; however, both ASV and SmartCare™ utilize more complex closed-loop algorithms compared to MMV [20]. SmartCare™ uses artificial intelligence, control theory and planning theory to implement a series of rules (IF specific conditions are met THEN explicit actions are implemented) with temporal reasoning emanating from expert opinion, physiologic studies and RCTs [47, 48]. ASV, while not based on artificial intelligence, utilizes a set of rules based on respiratory physiology and clinical management of patients on mechanical ventilation. In summary, closed-loop control is a general approach that has been implemented on commercially available systems in different ways (using different operating principles) and experimentally using novel approaches, such as fuzzy logic [49].

## Advantages and disadvantages of automated weaning systems

Automating the weaning process has several important advantages. First, with automation, weaning becomes interactive enabling patients to interact with the ventilator and to adapt ventilator output in accordance with their individual and instantaneous needs. Second, closed-loop technology permits mechanical ventilation to be titrated and adapted continuously during weaning. Consequently, weaning is not delayed or impeded by limited clinician availability in the busy ICU setting. Third, decision making during weaning is optimized by ventilator recognition of key events (e.g., SBT readiness). For these reasons, automated weaning holds promise as a way to reduce practice pattern variation and facilitate translation of new knowledge into practice to improve patient outcomes [46].

Currently available closed-loop systems have general and system-specific limitations. Despite being highly efficient in achieving predetermined targets, automated systems run the risk of relentlessly pursuing target values or responding to artifact. Moreover, developers of automated systems may be particular susceptible to the temptation to develop systems to translate complex physiologic models into oversimplified algorithms with limited clinical applications [50–52] and to manage all aspects of mechanical ventilation. To this end, the systems we reviewed endeavor to synthesize basic physiologic parameters into simple models which integrate clinical reasoning into algorithms that can be applied at the bedside. While some systems were developed to support patients requiring controlled or assisted ventilation, other systems were specifically developed for spontaneously breathing patients and to guide selected aspects of mechanical ventilation (e.g., weaning). Finally, these systems have not been fully tested in specific patient populations (with severe bronchospasm, abundant secretions, severe critical illness polyneuropathy or myopathy) which often prove challenging to wean from mechanical ventilation, regardless of the mode or strategy utilized [38].

With regard to specific system limitations, ASV assumes that optimal combinations of $V_T$ and RR represent *ideal* breathing patterns regardless of whether patients require full or assisted ventilation. With ASV, weaning can be impeded if the desired minute ventilation target is too high or in the setting of hyperventilation. In this circumstance, a stepwise reduction in the percentage (e.g., 60%) of the normal minute ventilation targeted typically allows spontaneous breathing to resume [31, 33, 34]. Since SmartCare™ is operationalized in PS mode, clinicians must exercise caution in sedating patients when using this strategy. If sedation administration results in a decreased RR, SmartCare™ may incorrectly classify the patient to be in the comfort zone (normal ventilation state) and decrease the assistance provided. Conversely, a high RR may not be due to "insufficient ventilation" and SmartCare™ may mistakenly increase the PS provided to agitated patients. Frequent reassessments of patient clinical status, respiratory parameters and $P_{ET}CO_2$ are advised to limit the risk for severe hypoventilation or hyperventilation with SmartCare™.

## Conclusion

Advanced closed-loop systems have heralded an exciting era of mechanical ventilation that aims to simplify ventilator management by making the weaning process interactive, responsive and adaptive. Whether automated weaning reduces weaning practice pattern variation and facilitates knowledge translation remains to be established. However, automation during weaning does not yet supersede the need for close patient observation and monitoring, nor does it supplant the need for clinicians to make important clinical judgments during weaning and regarding critical events such as readiness for extubation. The role for automation in weaning may be to complement the clinical acumen and care provided by clinicians in optimizing the *process* of delivering care to critically ill patients requiring invasive ventilation in the busy ICU setting. Additional high quality, clinical investigations are required to assess whether the promises of automation can be realized in various patient populations and practice settings, and to elucidate the impact of newer closed-loop systems on other important clinical outcomes.

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