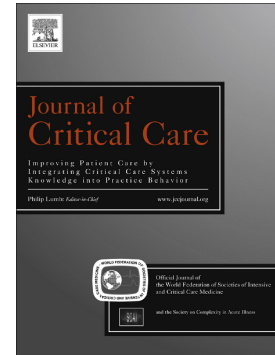


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Effects of staff training and electronic event monitoring on long-term adherence to lung-protective ventilation recommendations

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Abstract:

Purpose: To investigate long-term effects of staff training and electronic clinical decision support (CDS) on adherence to lung-protective ventilation recommendations.

Materials and Methods: In 2012, group instructions and workshops at two surgical intensive care units (ICUs) started, focusing on standardized protocols for mechanical ventilation and volutrauma prevention. Subsequently implemented CDS functions continuously monitor ventilation parameters, and from 2015 triggered graphical notifications when tidal volume (V_T) violated individual thresholds. To estimate the effects of these educational and technical interventions, we retrospectively analyzed nine years of V_T records from routine care. As outcome measures, we calculated relative frequencies of settings that conform to recommendations, case-specific mean excess V_T , and total ICU survival. **Results:** Assessing 571,478 V_T records from 10,241 ICU cases indicated that adherence during pressure-controlled ventilation improved significantly after both interventions; the share of conforming V_T records increased from 61.6% to 83.0% and then 86.0%. Despite increasing case severity, ICU survival remained nearly constant over time.

Conclusions: Staff training effectively improves adherence to lung-protective ventilation strategies. The observed CDS effect seemed less pronounced, although it can easily be adapted to new recommendations. Both interventions, which futures studies could deploy in combination, promise to improve the precision of mechanical ventilation.

Keywords:

clinical decision support, tidal volume, lung protective ventilation, ARDS, Arden Syntax

Funding and Conflicts of Interest:

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Abbreviations:

APACHE II	Acute Physiology and Chronic Health Evaluation II
ARDS	Acute Respiratory Distress Syndrome
CDS	Clinical Decision Support
PBW	Predicted Body Weight
PDMS	Patient Data Management System
V_T	Tidal Volume: gas volume moved into the patient by the ventilator with every breath

1. Introduction

1.1. Scientific background

On Intensive Care Units (ICUs), respiratory dysfunction due to several causes ranks among the most important clinical problems. Acute respiratory distress syndrome (ARDS) remains frequent and still results in a high mortality [1]. One of the essential parameters in mechanical ventilation is the tidal volume (V_T), defined as the gas volume the ventilator moves into the lungs during each respiratory cycle. Over the years, different strategies of adjusting V_T have been discussed [2]. In 1963, Bendixen et al. proposed the use of high V_T settings above 10 ml per kg predicted body weight (PBW) in order to prevent acidosis and atelectasis, and to improve oxygenation [3].

In later studies, however, such high V_T turned out to be harmful and to increase mortality [4] by causing “ventilator induced lung injury” [5], which led to the concept of the “baby lung” [6]. Special lung-protective ventilation strategies advise a lower V_T setting (6-8 ml/kg PBW) to reduce pulmonary side effects of mechanical ventilation and thus mortality [2]. This recommendation seems to protect not only patients with severe lung injuries, but anyone in need of mechanical ventilation [e.g. 7, 8, 9, 10, 11, 12]. Integrating these concepts into ICU routines, however, can be difficult and information-intensive insofar as frequently updated V_T settings have to consider patient-specific threshold parameters. Taking the importance of this parameter into account during everyday care depends on intensive staff training, while reminders and electronic support generally promise to improve awareness.

1.2 Rationale for the study

Accurate lung-protective ventilation requires calculating patient-specific V_T recommendations from PBW, which in turn is estimated by a linear formula from patient sex and height [2, 13]. In addition to potential side effects of low-volume ventilation, the “difficulty [of] calculating tidal volume” is seen as a potential obstacle for a systematic adherence in daily practice [14]. Moreover, the parameters of mechanical ventilation have to be closely monitored over time and if necessary adjusted, because dynamic factors such as supine or prone positioning, fluid balance and edema, neuromuscular blocking, and sedation can influence thoracic compliance and therefore V_T (depending on the ventilation mode used). These determinants certainly contribute to the observation that “the protective ventilation strategy is often under-utilized as a therapeutic option, even in ARDS” [7].

Some organizational and educational efforts have aimed to consistently implement these lung-protective strategies in routine intensive care, but have yet produced only moderate clinical effects [14, 15, 16, 17]. In previous studies of clinical decision support (CDS) for mechanical ventilation, Eslami et al. had reported that providing individual V_T calculations as part of the order entry process led to a more consistent application of lung-protective protocols in patients who were ventilated for more than 24 hours, although adherence appeared to depend on the implemented CDS communication style [18, 19]. The authors interpret a presumed trade-off between workflow

intrusiveness and clinical effectiveness, and conclude that alternative CDS designs should be examined [19].

In contrast to these published CDS functions that had been integrated with patient-specific data entry, clinical event monitoring is rather geared to *'tirelessly'* watch over clinical databases, and if necessary to communicate notifications beyond the context of individual medical records [20]. A review of CDS features enlisted an automatic provision among the determinants of an improved clinical practice [21]. Therefore, and because a continuous supervision appears to resonate with therapeutic requirements, we hypothesized that event monitoring might likewise facilitate putting sustained lung-protective ventilation into practice.

To comparatively estimate long-term effects of staff training and CDS-based graphical notifications, we retrospectively analyzed adherence to lung-protective ventilation recommendations at two surgical ICUs.

2. Material and Methods

2.1 Setting

Erlangen University Hospital is a tertiary care facility in southern Germany with approximately 1,370 beds. This study took place on two surgical ICUs with collectively 35 beds, which in 2015 treated 2,400 adult patients and in total administered approximately 87,000 ventilator hours. At the end of 2006, both ICUs were equipped with a commercial patient data management system (PDMS, Integrated Care Manager®, Dräger Medical, Lübeck, Germany), which is used to document various patient attributes, such as vital signs, medication data, nursing activities, laboratory results, and blood gas analysis [22].

This application has already been used for studying ICU documentation [23], workflows [24] and finances [25], and served as the basis for implementing a CDS platform whose technical characteristics have been reported previously [26, 27, 28]. This CDS infrastructure builds on Arden Syntax, which has been purposefully designed to facilitate a modular and shareable definition of automated reasoning in support of particular clinical decisions [29]. The PDMS supports diverse data processing tasks, such as automated calculations of Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. All ventilators have interfaces with the PDMS, enabling the automatic storage of ventilation settings and associated measurements.

2.2 Conventional training intervention

In response to formerly published recommendations on mechanical ventilation, ICU nurses and a senior physician convened earlier to standardize locally adapted protocols concerning lung-protective ventilation. Based on the developed documents, a series of training sessions for ICU staff was initiated at the beginning of 2012. These consisted of one-hour instructions in groups of approximately 20 persons, which in sum were attended by around 109 nurses and physicians, from a total of approximately 150. These courses were held again in August 2012, and then reached 52 staff members from 150. Tuition was augmented with several four-hour workshops, where another 52 workers participated, with yearly lessons (each reaching approximately 80 people) among other things dedicated to V_T settings, as well as with online manuals provided to instruct employees when they rotated to either of the two ICUs.

These educational interventions addressed standard operating procedures for mechanical ventilation, essential settings such as limited peak pressure, continuous positive airway pressure, V_T , respiratory rate, and inspired oxygen fraction. Training repeatedly focused on clinical benefits of

avoiding high- V_T ventilation, and explained how to calculate individually recommended V_T maxima according to 8 ml/kg PBW, while weight was to be estimated as a linear function of height and sex, in conformance with applicable guidelines [2].

2.3. CDS intervention

Even after the training intervention, daily experience suggested that V_T settings might often remain too high. This circumstantial evidence prompted the alternative consideration and prototypical implementation of an Arden-based CDS module for monitoring and if necessary notifying staff about potential non-adherence. Like previous applications [18, 19], we assumed that individual V_T targets should follow PBW-dependent ventilation requirements. The developed triggering mechanism thus implements the established linear functions in order to automatically personalize V_T thresholds from PDMS records.

Insofar as unspecific CDS messages can entail that nurses and physicians begin to ignore or override notifications in practice [30], we aimed to minimize such ‘*alert fatigue*’ by deliberately restricting criteria to situations where the benefits of lowering V_T seemed relatively unambiguous. This was realized by relaxing recommended thresholds by 10%, so that only V_T settings in excess of 8.8 ml/kg PBW could effectively trigger alerts.

To keep temporary violations from provoking inconsequential notifications, the CDS function analyzes recent case-specific records in order to ensure that either the preceding V_T record or the previous 6-hour average also breached 8.8 ml/kg. To further prevent false positive messages, the trigger mechanism automatically monitors whether current settings belong to a previously defined selection of pressure-controlled ventilation modes (technically encoded as a list of trademarked mode notations).

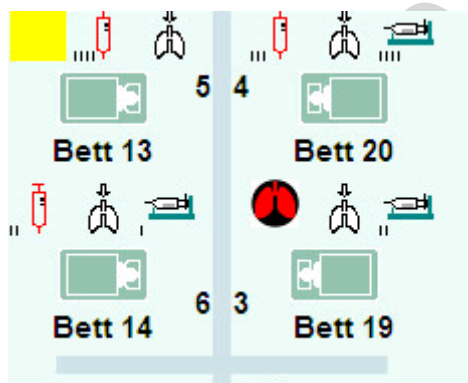


Figure 1: PDMS detail of a ward overview. The round “red lung” overlay signals that the event monitor detected a violation of recommended V_T maxima for the patient in bed 19. The other displayed icons are configured to graphically summarize various patient features with a general relevance for clinical management.

Since the intrusiveness of generated warnings may hamper effective clinical responses [30], we specifically designed messages to avoid workflow interruptions as far as possible. Notifications were therefore communicated via warning icons, which the CDS mechanism superimposed as necessary on a patient-specific graphical representation of the central ward overview (see figure 1). This rather subtle communication style does not require that staff members occupy themselves with active data entry into patient-specific PDMS records, but still promises that those who are present on the ward may become aware relatively fast.

When the developed alerting function was activated on two surgical ICUs in February 2015, nurses and physicians were briefed via hand-outs, via email, and via brief demonstrations; this introductory information explained the motivation for the intervention, the developed functionality, suitable interpretations of the warning symbols, as well as the background of the accompanying observational study.

2.4 Study design and participants

To retrospectively investigate potential effects of the described educational and technical lung-protective interventions on clinical practice, we exported and analyzed basic patient features and ventilator parameters from the PDMS. Among surgical ICU patients who had been treated between January 2007 and February 2016, case-specific datasets were included in the analysis if certain ventilation modes as well as simultaneous V_T records had been documented on at least four different points in time, and if PBW could be recalculated from available height and sex attributes. In addition to a selection of pressure-controlled ventilation modes (which potentially triggered notifications), we also analyzed the development of tidal volumes that were recorded during spontaneous assisted modes (which could not trigger alerts), where the relationship between ventilator parametrization and measurable V_T is more indirect.

The selected ICU cases were then subdivided according to both lung-protective interventions that had been introduced at the time of individual ICU admissions. We interpret the initial five-year phase after PDMS deployment as baseline (Jan 2007 – Dec 2011). During the following three-year interval, the educational intervention has been introduced, but the CDS function was not yet implemented (Jan 2012 – Feb 2015). Between the middle of February 2015 and February 2016, staff training as well as automated V_T event monitoring was activated. Figure 2 summarizes the selection of PDMS cases and their distribution across these three phases.

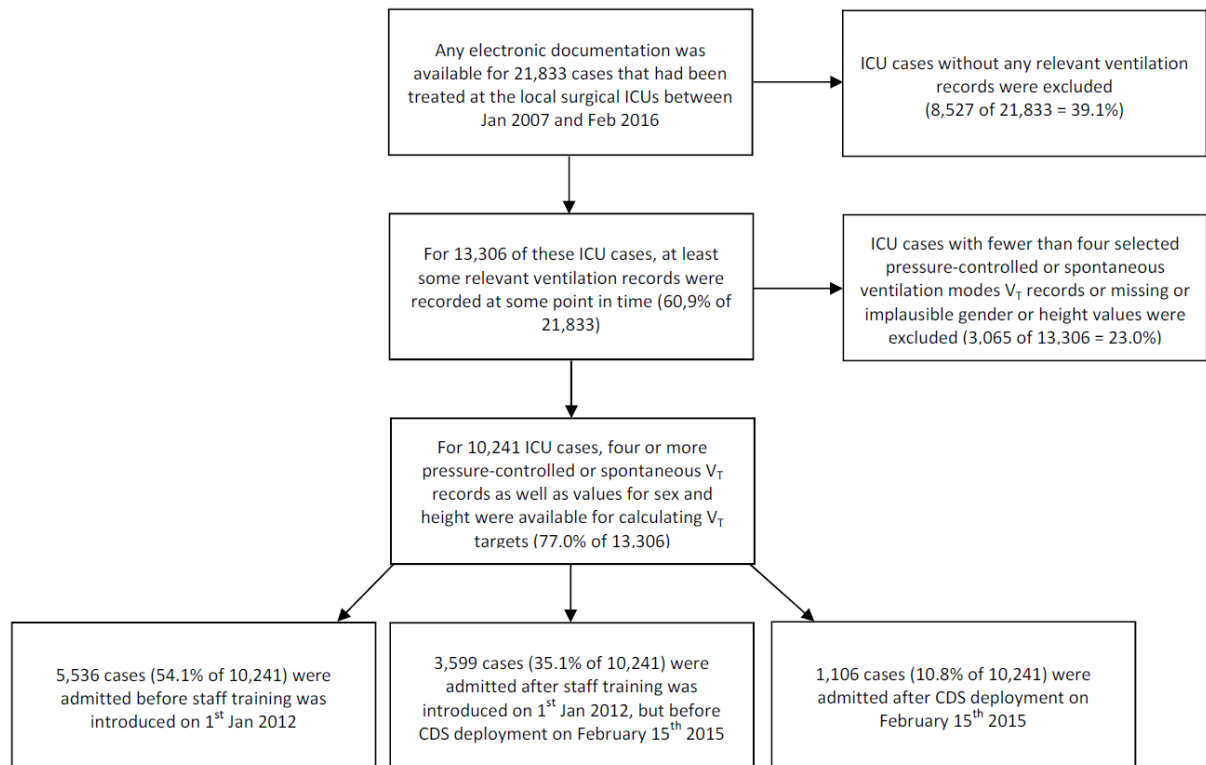


Figure 2: Overview of the selection of ICU cases for retrospective analysis and subdivision into three cohorts.

2.5 Outcome measures and statistical analyses

To estimate effects on adherence to lung-protective ventilation, we calculated relative frequencies of ventilator settings that would conform to individual recommendations, case-specific mean excess V_T (i.e., above individual thresholds), as well as total ICU survival (regardless of length of stay) in electronic PDMS exports. Quantifying adherence within various patterns of individual V_T readings should obviously take into account that we would feasibly expect both the duration as well as the severity of any threshold violation to negatively affect clinical outcomes.

To avoid the loss of information that would originate from simplifying individual V_T time series into ‘how many’ readings should be considered ‘too high’, we quantified non-adherence along the lines of the ‘hyperglycaemic index’, which Vogelzang et al. [31] had proposed as the average area of the blood glucose curve above a presumed upper threshold. By analogy, we summarized excess V_T as the average area of each case-specific V_T time series above a presumed personalized upper threshold of 8.8 ml/kg PBW. This method yields the advantage of monotonically reflecting the duration as well as the severity of any V_T elevation; when none of the V_T readings oversteps case-specific limits, this metric assumes a value of zero, which is consistent with our intuition that in such situations no V_T excess is present.

All statistical analyses based on PDMS exports were performed in R 3.3. Exact temporal calculations were achieved by converting timestamp-representing character sequences via `strptime()`. Potential associations in frequency tables were evaluated with `fisher.test()` or with `chisq.test()`, depending on the number of observations. We compared sets of sortable (i.e., ordinal) or metric observations using `quantile()`, `mean()`, `boxplot()` and `wilcox.test()`. Multivariate linear models of the ranks of excess V_T estimates were fitted with `lm()`.

3. Results

3.1 Patient data overview

A total of 10,241 patients who were treated at both local surgical ICUs between January 2007 and February 2016 fulfilled our described inclusion criteria concerning data completeness and minimum ventilation records. Based on admission dates, 5,536 case records were assigned to the first study phase 1 (baseline), 3,599 to phase 2 (after the educational intervention), and 1,106 to phase 3 (after the CDS function was activated). Table 1 summarizes the basic characteristics of these patient groups.

Approximately two thirds of cases were male, with moderate fluctuations. About one quarter of cases was on admission younger than 59 years, while another 25% were older than 76 years. The distribution of the length of ICU stays was strongly asymmetric around a median of around 44 hours, insofar as a dense left tail concentrated a high number of short postoperative stays, while a few cases experienced rather protracted recoveries.

	Phase 1	Phase 2	Phase 3	P-Value
Admission period	Jan 2007 – Dec 2011	Jan 2012 – Jan 2015	Feb 2015 - Feb 2016	
Number of cases under ventilation	5,536 (54.1% of 10,241)	3,599 (35.1% of 10,241)	1,106 (10.8% of 10,241)	
Gender (% male)	3,735 (67.5% of 5,536)	2,521 (70.0% of 3,599)	758 (68.5% of 1,106)	0.035 *
Age on admission (years)	69.2 [59.4 - 75.9] μ 66.7 \pm 13.1	69.5 [59.0 - 76.2] μ 66.7 \pm 13.6	68.1 [58.1 - 76.2] μ 66.2 \pm 13.4	0.443 and 0.136 §
Height (cm)	170 [165 - 177] μ 170.2 \pm 9.8	172 [165 - 178] μ 171.0 \pm 9.2	172 [165 - 178] μ 171.0 \pm 9.7	0.001 and 0.665 §
Length of ICU stay (hours)	44.2 [22.1 - 100.5] μ 120.4 \pm 246.5	43.0 [21.7 - 115.4] μ 128.6 \pm 263.6	44.7 [21.3 - 135.1] μ 138.9 \pm 263.4	0.651 and 0.437 §
APACHE II scores (available for 5,799 cases)	19 [16 - 24] μ 20.2 \pm 6.9 (2,882 cases)	23 [19 - 27] μ 23.6 \pm 6.5 (2,215 cases)	24 [20 - 28] μ 24.7 \pm 6.5 (701 cases)	< 0.001 and < 0.001 §
Duration of ventilation (hours)	10.3 [5.2 - 47.7] μ 83.4 \pm 229.6	8.6 [4.7 - 45.5] μ 86.5 \pm 242.6	10.2 [4.9 - 66.1] μ 92.5 \pm 228.1	< 0.001 and 0.012 §
Cases with >24 hours ventilation (%)	1,783 (32.2% of 5,536)	1,117 (31.0% of 3,599)	392 (35.4% of 1,106)	0.024 *

Table 1: Basic characteristics of 10,241 analyzed cases. * *fisher.test()*, median [interquartile range] μ mean \pm standard deviation, § *wilcox.test()* phase 1 vs. phase 2 and phase 2 vs. phase 3.

Average patient height appeared to increase slightly between phase 1 and phase 2, which may be attributable to a growing proportion of male patients. Case severity as measured by APACHE II scores increased moderately over time. During the last study phase, a somewhat higher fraction of patients under mechanical ventilation appeared to require it for longer than 24 hours.

3.2 Development of outcome parameters

In total, we included 571,478 V_T observations in the analysis, which amount to an average of 55.8 V_T values per case. Timestamp differences between the earliest and the latest patient-specific V_T records suggest that the analyzed cohort collectively accumulated 875,570 ventilation hours, although their distribution across the 10,241 cases was quite skewed. Mean ventilation as measured by the difference between the earliest and latest case-specific V_T record lasted for around 85.5 hours

(3.6 days), with the correspondingly estimated measurement intervals between successive V_T records averaging approximately 92 minutes.

Logfile analysis indicated that the event monitor was technically available 95.2% of the time after activation. Warning icons were displayed in 1,782 situations, and were thus triggered for 354 of those 1,059 cases in question (33%) who received pressure-controlled ventilation between February 2015 and February 2016.

As is shown in table 2, the proportion of 'conforming' V_T measurements (i.e., those $<8.8\text{ml/kg PBW}$ that could not trigger CDS alerts) during pressure-controlled ventilation increased from 61.6% before the educational intervention to 83.0%, followed by a further modest improvement after CDS activation to 86.0%. Likewise, the corresponding percentage of V_T settings that exceeded 150% of individual maxima decreased twice. When spontaneous assisted modes were applied, the development was more heterogeneous insofar as the share of conforming V_T settings first increased and then decreased moderately.

According to case-specific quantitative summaries of ventilation settings, excess V_T during pressure-controlled ventilation decreased markedly after the educational intervention (see figure 3). When the event monitor was subsequently switched on, the distribution of case-specific excess V_T displayed no comparable further improvement. Figure 3 also illustrates that any changes concerning spontaneous modes were much smaller than the relatively pronounced improvement after the educational intervention during pressure-controlled ventilation. Another analysis of V_T settings that differentiated the case-specific time that has elapsed after the initiation of mechanical ventilation indicated that high-volume V_T settings were less frequent during long-term ventilation (see supplement).

	Phase 1	Phase 2	Phase 3	P-Value
Total V _T records during pressure-controlled modes	156,195 (60.3% of 259,017)	76,598 (29.6% of 259,017)	26,224 (10.1% of 259,017)	
Total V _T records during spontaneous modes	147,793 (47.3% of 312,461)	123,272 (39.5% of 312,461)	41,396 (13.2% of 312,461)	
Conforming V _T records (< 8.8 ml/kg PBW) during pressure-controlled modes	96,212 (61.6% of 156,195)	63,562 (83.0% of 76,598)	22,558 (86.0% of 26,224)	< 0.001 and < 0.001 ‡
V _T records above 150% of individual thresholds during pressure-controlled modes	3,118 (2.0% of 156,195)	602 (0.8% of 76,598)	168 (0.6% of 26,224)	< 0.001 and 0.021 ‡
Case-specific mean V _T excess > 8.8ml/kg in ml during pressure-controlled modes ¶	12.8 [0.2 - 51.3] µ 37.3 ± 60.5 (5,316 cases)	1.2 [0.0 - 19.2] µ 20.6 ± 62.3 (3,472 cases)	0.9 [0.0 - 18.1] µ 19.6 ± 48.5 (1,059 cases)	< 0.001 and 0.672 §
Case-specific mean V _T excess > 8.8ml/kg in ml during pressure-controlled modes among cases with >24 hours ventilation ¶	15.6 [2.5 - 49.1] µ 34.5 ± 50.2 (1,697 cases)	1.9 [0.0 - 14.1] µ 17.9 ± 82.6 (1,056 cases)	2.0 [0.0 - 15.2] µ 16.5 ± 47.7 (373 cases)	< 0.001 and 0.975 §
Conforming V _T records (< 8.8 ml/kg PBW) during spontaneous modes	96,749 (65.5% of 147,793)	85,348 (69.2% of 123,272)	27,365 (66.1% of 41,396)	< 0.001 and < 0.001 ‡
V _T records above 150% of individual thresholds during spontaneous modes	5,946 (4.0% of 147,793)	4,093 (3.3% of 123,272)	1,643 (4.0% of 41,396)	< 0.001 and < 0.001 ‡
Case-specific mean V _T excess > 8.8ml/kg in ml during spontaneous modes ¶	9.8 [0.0 - 73.3] µ 59.6 ± 116.8 (4,958 cases)	12.1 [0.0 - 76.1] µ 63.2 ± 118.9 (3,309 cases)	14.3 [0.0 - 75.7] µ 56.9 ± 96.4 (1,001 cases)	0.021 and 0.471 §
Case-specific mean V _T excess > 8.8ml/kg in ml during spontaneous modes among cases with >24 hours ventilation ¶	18.0 [1.6 - 64.7] µ 52.1 ± 104.5 (1,613 cases)	14.1 [0.9 - 55.6] µ 45.6 ± 80.4 (1,056 cases)	18.2 [2.0 - 62.0] µ 44.8 ± 70.8 (369 cases)	0.057 and 0.204 §
Total ICU nonsurvival of patients under mechanical ventilation (%)	486 (8.8% of 5,536)	313 (8.7% of 3,599)	99 (9.0% of 1,106)	0.960 *
Total ICU nonsurvival among cases with >24 hours ventilation (%)	390 (21.9% of 1,783)	250 (22.4% of 1,117)	75 (19.1% of 392)	0.397 *

Table 2: Clinical outcomes and summaries of ventilation parameters calculated from 571,478 V_T records. * fisher.test(), median [interquartile range] µ mean ± standard deviation, § wilcox.test() phase 1 vs. phase 2 and phase 2 vs. phase 3, ¶ available for subsets of cases, ‡ chisq.test() phase 1 vs. phase 2 and phase 2 vs. phase 3.

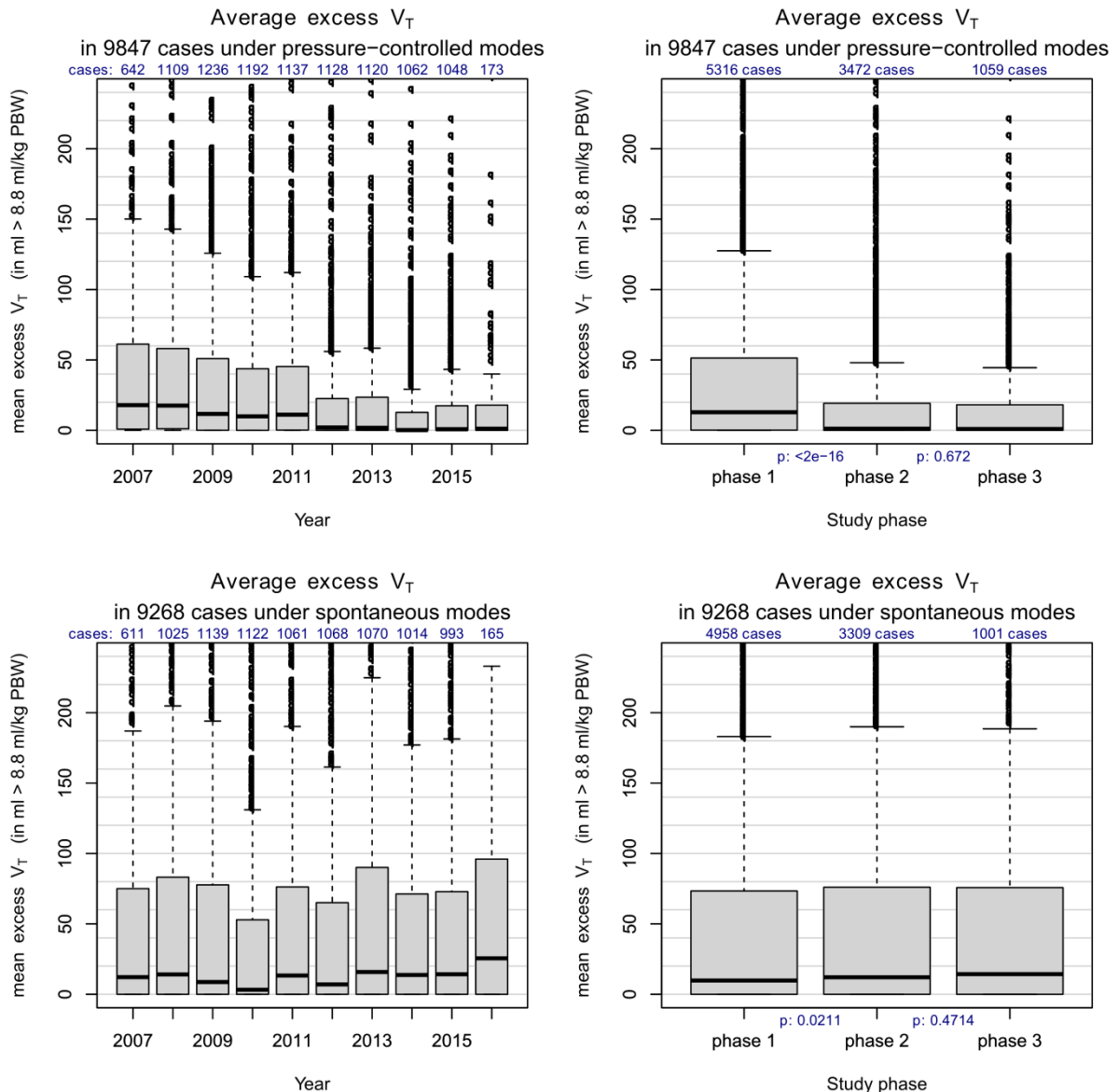


Fig. 3: Development of excess V_T above 8.8 ml/kg PBW during pressure-controlled and spontaneous ventilation.

According to multivariate linear models of the ranks of excess V_T , adherence under pressure-controlled ventilation improved significantly between phases 1 and 2, while the corresponding difference between phases 2 and 3 was not significant (see supplement). When no interaction term for height and sex was included, excess V_T was unexpectedly lower for taller patients and for women; in a model that accounted for potential interaction between height and sex, women as well as smaller patients experienced significantly more V_T excess. These complex relationships might indicate that actual clinical requirements could be more intricate than PBW-based V_T targets that are estimated as linear functions of sex and height. During pressure-controlled ventilation neither age on admission, APACHE II scores, length of ICU stay, nor the duration of ventilation displayed notable associations with excess V_T . No study phases were associated with excess V_T under spontaneous modes, but patient sex and height were related in the same direction like under pressure-controlled modes.

During the three study phases, overall ICU survival remained relatively constant, including among patients who received ventilation for longer than 24 hours, even though severity as measured by the distribution of APACHE II scores increased moderately over time. We could not identify any available PDMS data that would have been suitable for a selective subgroup analysis of pulmonary complications and ventilator-associated mortality.

4. Discussion

It has been reported that adherence to the ARDSNetwork recommendations for lung-protective ventilation can be inconsistent, and that specific interventions should target an improved application in clinical practice [14, 15, 16, 32, 33]. We thus analyzed adherence at two surgical ICUs over the past years in order to judge whether two interim interventions – staff training and implementation of CDS-based event monitoring – had any effect on ventilation settings.

Our retrospective analysis had to confront the problem that putting the initial educational intervention into practice actually took some time because of the number of persons who had to be trained, a process which in fact continues to date. Nevertheless, for analytical purposes, we had to simplify this ongoing organizational procedure in order to delimit comparable periods of time before and after instructions commenced.

The need for repeated staff training and the associated expenditures in time and money [34] then originated the idea of an automatic electronic monitoring of V_T settings. Motivated by earlier comparable investigations [18, 35], we subsequently developed a specific notification module based on the local CDS platform [26, 27]. The deployment of this monitoring function took considerably less effort than the described staff training, and could be easily activated at a defined point in time.

Interpretation of main observations

We interpret that it is likely that the initial intervention – conventional training of medical staff – materially improved adherence to recommended V_T maxima during pressure-controlled ventilation. The necessity and effectiveness of repeated training, teaching and standardization of such procedures has been investigated before [14, 15, 16, 32, 33], so this finding may not be surprising.

Another interesting observation concerns a reduced median duration of ventilation in phase 2 (from 10.3h down to 8.6h, see table 1), which seems more remarkable in light of increasing median APACHE II scores (from 19 to 23). This reduction of ventilation hours may in retrospect be attributable to other parts of the introduced training program, which aimed to accelerate weaning from mechanical ventilation. The observed relatively constant V_T settings under spontaneous assisted ventilation may be due to the fact that local staff training prioritized V_T settings under controlled ventilation, therefore a relevant change in other modes seems less likely.

The second phase after the institution of staff training simultaneously served as the comparison group for estimating the potential additional effect of the subsequently deployed alerting system – the primary innovation in this study. In relation to previous CDS functions for supporting lung-protective ventilation, our application was specifically geared to achieve a high degree of automation. This way, notifications can be triggered without the need of repeated user interactions with the PDMS, as long as patients' height and sex have been entered once as the basis for estimating individual V_T thresholds.

The advanced integration and automatization of our system targets a seamless V_T monitoring as well as a low number of alarms, thus allowing for mostly undisturbed ICU work routines. Several CDS functions have been described and investigated in practice [18, 19, 35, 36, 37, 38], although we interpret that earlier applications involved relatively tighter integration with manual

data entry tasks. Because of our careful embedding into work processes, in the run-up to the CDS activation we had actually expected to see some further improvements of V_T settings. In fact, after event monitoring was switched on in February 2015, the quantitative outcome parameter of excess V_T during pressure-controlled ventilation displayed no further reduction that would compare in magnitude to the one that earlier followed on the educational intervention. The proportion of single V_T records that complied with case-specific thresholds, however, improved modestly (from 83.0% under 8.8 ml/kg PBW up to 86.0%), as did the proportion that at least fell below 150% of these maxima (from 0.8% down to 0.6%). The clinical relevance of these rather subtle shifts seems difficult to gauge.

Among the potential explanations for the sobering observation that our carefully designed automated monitoring application admittedly produced no further substantial improvements of V_T parameters, one reason could be that the previous educational intervention has already largely exhausted clinically achievable improvements. Another interpretation would be that the graphical notifications –which automatically disappear after a period of 20 minutes unless new data prompt their reappearance– had been designed in a too reticent communications style, and in some situations could have been simply ignored in practice.

Another reason, supported by circumstantial observations, could be some staff members (despite repeated instructions) may not have been always fully aware of the meaning of and adequate responses to the graphical warning symbols. A different interpretation could be that since any CDS method will always build on formalized generalizations that cannot fully capture all information that may be relevant in every individual instance, clinicians at the bedside may in some situations also have consciously decided not to respond to graphical alerts due to particular clinical reasons, such as current hypercapnia or hypoxia.

4.1 Strengths and weaknesses of the study

Over the nine-year period that we retrospectively studied, various features of patient management and patient care may well have changed, so attribution of any shifts in outcomes to the described interventions should be inferred with caution. On the other hand, we were able to automatically analyze a large collective of patients with a substantial number of V_T measurements, which we see as potentially representative for various clinical settings.

The local general prerequisites, however, also differ from the ones reported 2012 by Eslami et al. insofar as our analyzed case sets consisted of surgical ICU populations, while a majority of previously investigated patients were predominantly medical cases; this fundamental difference between the studied populations has likely contributed to a relatively shorter distribution of ventilation hours at our local surgical ICUs, and may simultaneously undermine the general comparability between pulmonary risk profiles, complication frequencies, and CDS effects.

Our novel CDS-module which automatically monitors V_T settings – with a patient-individual calculation of V_T limits and graphical notifications that do not depend on active user actions – can be interpreted as unique feature. The automatic background computations were designed to produce only a reduced number of specific alarms – which can be seen as substantial potential advance in monitoring of mechanical ventilation.

On the one hand, the observation that ICU survival remained mostly unchanged over the years could also be seen as a failure to achieve relevant improvements. In light of an exacerbating case severity as measured by APACHE II scores between study phases, however, holding ICU outcomes relatively constant might also be consistent with gradual therapeutic improvements. In this retrospective analysis based on reutilized PDMS records from everyday care, adequate control of various potential confounders remains inherently difficult. On the other side, this retrospective single-center study design with three study phases with varying duration and case numbers was certainly oriented towards achieving a cost-effective study completion based on a relatively subtle workflow modification. In theory, more resources could be employed in order to examine such interventions

more thoroughly, for example by widening clinical settings to several sites, or by simultaneously testing alternative CDS designs with alternative communication styles via crossover trials.

4.2 Outlook

The real effects of CDS functions on the quality of care of critically ill patients are known to be difficult to assess. We see it as plausible that obtaining material clinical benefits via advanced CDS functions may increasingly depend on more complex underlying models. Since advanced automated analyses of vast PMDS data could in the future give rise to data-driven refinements of alerting criteria, and since triggered notifications could also feasibly be communicated in various other formats, such as via increasingly adopted wall-mounted displays or widespread handheld devices, the scope for promising alternative investigations in this context seems vast.

5. Conclusion

On ICUs adherence to recommended mechanical ventilation with low tidal volume can still be low. Staff training, protocols, standardization and other actions to improve this situation are highly effective but complex and need a repetitive effort. CDS promises to facilitate adherence, especially in larger teams where repeated staff training requires enormous resources. Once implemented, a CDS – can also be updated easily to new recommendations or to changing limits, thereby avoiding or at least reducing the need of repeated staff training. A seamless monitoring of ventilator parameters can thus help making mechanical ventilation more precise and its application safer for critically ill patients. Maybe the combination of both – education and electronic decision support – are the bundle of measures needed to achieve a lasting effect.

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8. Ethics committee approval

The Research Ethics Committee of the Faculty of Medicine, Friedrich-Alexander University Erlangen-Nuremberg, approved this study.

9. Conflicts of interest

No author reports a conflict of interest regarding the subject of this publication.

10. References

- [1] Villar J, Blanco J, Kacmarek RM. Current incidence and outcome of the acute respiratory distress syndrome. *Curr Opin Crit Care* 2016;22:1-6.
- [2] The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301-8.
- [3] Bendixen HH, Hedley-Whyte J, Laver MB. Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. *N Engl J Med* 1963;269:991-6.

- [4] Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, Kairalla RA, Deheinzelin D, Munoz C, Oliveira R, Takagaki TY, Carvalho CR. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med* 1998;338:347-54.
- [5] Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998;157:294–323.
- [6] Gattinoni L, Marini JJ, Pesenti A, Quintel M, Mancebo J, Brochard L. The "baby lung" became an adult. *Intensive Care Med* 2016;42:663-73.
- [7] Lellouche F, Lipes J. Prophylactic protective ventilation: lower tidal volumes for all critically ill patients?. *Intensive Care Med* 2013;39:6-15.
- [8] Hemmes SN, Severgnini P, Jaber S, Canet J, Wrigge H, Hiesmayr M, Tschernko EM, Hollmann MW, Binnekade JM, Hedenstierna G, Putensen C, de Abreu MG, Pelosi P, Schultz MJ. Rationale and study design of PROVHILLO - a worldwide multicenter randomized controlled trial on protective ventilation during general anesthesia for open abdominal surgery. *Trials* 2011;12:111.
- [9] Schultz MJ, Haitsma JJ, Slutsky AS, Gajic O. What tidal volumes should be used in patients without acute lung injury?. *Anesthesiology* 2007;106:1226–1231.
- [10] Guay J, Ochroch EA. Intraoperative use of low volume ventilation to decrease postoperative mortality, mechanical ventilation, lengths of stay and lung injury in patients without acute lung injury. *Cochrane Database Syst Rev* 2015;12:CD011151.
- [11] Park SH. Perioperative lung-protective ventilation strategy reduces postoperative pulmonary complications in patients undergoing thoracic and major abdominal surgery. *Korean J Anesthesiol* 2016;69:3-7.
- [12] Hubmayr RD. Point: is low tidal volume mechanical ventilation preferred for all patients on ventilation? Yes. *Chest* 2011;140:9–11.
- [13] Linares-Perdomo O, East TD, Brower R, Morris AH. Standardizing Predicted Body Weight Equations for Mechanical Ventilation Tidal Volume Settings. *Chest* 2015;148:73-8.
- [14] Rubenfeld G, Caldwell E, Hudson L. Publication of study results does not increase use of lung protective ventilation in patient with acute lung injury. *Am J Respir Crit Care Med* 2001;163:A295.
- [15] Wolthuis EK, Korevaar JC, Spronk P, Kuiper MA, Dzoljic M, Vroom MB, Schultz MJ. Feedback and education improve physician compliance in use of lung-protective mechanical ventilation. *Intensive Care Med* 2005;31:540-6.
- [16] Young MP, Manning HL, Wilson DL, Mette SA, Riker RR, Leiter JC, Liu SK, Bates JT, Parsons PE. Ventilation of patients with acute lung injury and acute respiratory distress syndrome: has new evidence changed clinical practice?. *Crit Care Med* 2004;32:1260-5.
- [17] Kalhan R, Mikkelsen M, Dedhiya P, Christie J, Gaughan C, Lanken PN, Finkel B, Gallop R, Fuchs BD. Underuse of lung protective ventilation: analysis of potential factors to explain physician behavior. *Crit Care Med* 2006;34:300-6.
- [18] Eslami S, de Keizer NF, Abu-Hanna A, de Jonge E, Schultz MJ. Effect of a clinical decision support system on adherence to a lower tidal volume mechanical ventilation strategy. *J Crit Care* 2009;24:523-9.
- [19] Eslami S, Abu-Hanna A, Schultz MJ, de Jonge E, de Keizer NF. Evaluation of consulting and critiquing decision support systems: effect on adherence to a lower tidal volume mechanical ventilation strategy. *J Crit Care* 2012;27:425.e1-8.
- [20] Hripcsak G, Clayton PD, Jenders RA, Cimino JJ, Johnson SB. Design of a clinical event monitor. *Comput Biomed Res* 1996;29:194-221.

- [21] Loya SR, Kawamoto K, Chatwin C, Huser V. Service oriented architecture for clinical decision support: a systematic review and future directions. *J Med Syst* 2014;38:140.
- [22] Castellanos I, Bürkle T, Prokosch HU, Schüttler J. Concept for the hospital-wide implementation of a patient data management system at a large clinical center-an interdisciplinary challenge. *Anästh Intensivmed* 2009;50:618–29.
- [23] Castellanos I, Ganslandt T, Prokosch HU, Schüttler J, Bürkle T. Implementation of a patient data management system. Effects on intensive care documentation. *Anaesthesist* 2013;62:887–897.
- [24] Bürkle T, Castellanos I, Tech H, Prokosch HU. Implementation of a patient data management system - an evaluation study of workflow alterations. *Stud Health Technol Inf* 2010;160:1256–60.
- [25] Castellanos I, Schüttler J, Prokosch HU, Bürkle T. Does introduction of a Patient Data Management System (PDMS) improve the financial situation of an intensive care unit? *BMC Med Inform Decis Mak* 2013;13:107.
- [26] Kraus S, Castellanos I, Toddenroth D, Prokosch HU, Bürkle T. Integrating Arden-Syntax-based clinical decision support with extended presentation formats into a commercial patient data management system. *J Clin Monit Comput* 2014;28:465–73.
- [27] Castellanos I, Kraus S, Toddenroth D, Prokosch HU, Bürkle T. Using Arden Syntax Medical Logic Modules to reduce overutilization of laboratory tests for detection of bacterial infections-Success or failure? *Artif Intell Med* 2015;25:S0933-3657. <http://dx.doi.org/10.1016/j.artmed.2015.09.005>.
- [28] Kraus S, Drescher C, Sedlmayr M, Castellanos I, Prokosch HU, Toddenroth D. Using Arden Syntax for the creation of a multi-patient surveillance dashboard. *Artif Intell Med* 2015, <http://dx.doi.org/10.1016/j.artmed.2015.09.009>.
- [29] Hripcsak G, Ludemann P, Pryor TA, Wigertz OB, Clayton PD. Rationale for the Arden Syntax. *Comput Biomed Res* 1994;27:291-324.
- [30] Van der Sijs H, Aarts J, Vulto A, Berg M. Overriding of drug safety alerts in computerized physician order entry. *J Am Med Inform Assoc* 2006;13:138-47.
- [31] Vogelzang M, van der Horst ICC, Nijsten MWN. Hyperglycaemic index as a tool to assess glucose control: a retrospective study. *Crit Care* 2004;8:R122-R127.
- [32] Weiss CH, Baker DW, Weiner S, Bechel M, Ragland M, Rademaker A, Weitner BB, Agrawal A, Wunderink RG, Persell SD. Low Tidal Volume Ventilation Use in Acute Respiratory Distress Syndrome. *Crit Care Med* 2016;44:1515-22.
- [33] Nota C, Santamaria JD, Reid D, Tobin AE. The impact of an education program and written guideline on adherence to low tidal volume ventilation. *Crit Care Resusc* 2016;18:174-80.
- [34] Cooke CR, Kahn JM, Watkins TR, Hudson LD, Rubenfeld GD. Cost-effectiveness of implementing low-tidal volume ventilation in patients with acute lung injury. *Chest* 2009;136:79-88.
- [35] Bagga S, Paluzzi DE, Chen CY, Riggio JM, Nagaraja M, Marik PE, Baram M. Better ventilator settings using a computerized clinical tool. *Respir Care* 2014;59:1172-7.
- [36] Garg AX, Adhikari NK, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, Sam J, Haynes RB. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. *JAMA* 2005;293:1223-38.
- [37] East TD, Heermann LK, Bradshaw RL, Lugo A, Sailors RM, Ershler L, Wallace CJ, Morris AH, McKinley B, Marquez A, Tonnesen A, Parmley L, Shoemaker W, Meade P, Thaut P, Hill T, Young M, Baughman J, Olterman M, Gooder V, Quinn B, Summer W, Valentine V, Carlson J, Steinberg K. Efficacy of computerized decision support for mechanical ventilation: results of a prospective multi-center randomized trial. *Proc AMIA Symp* 1999:251-5.

- [38] McKinley BA, Moore FA, Sailors RM, Cocanour CS, Marquez A, Wright RK, Tonnesen AS, Wallace CJ, Morris AH, East TD. Computerized decision support for mechanical ventilation of trauma induced ARDS: results of a randomized clinical trial. *J Trauma* 2001;50:415-24.

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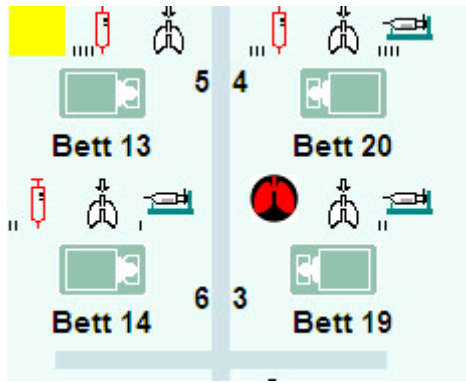


Figure 1

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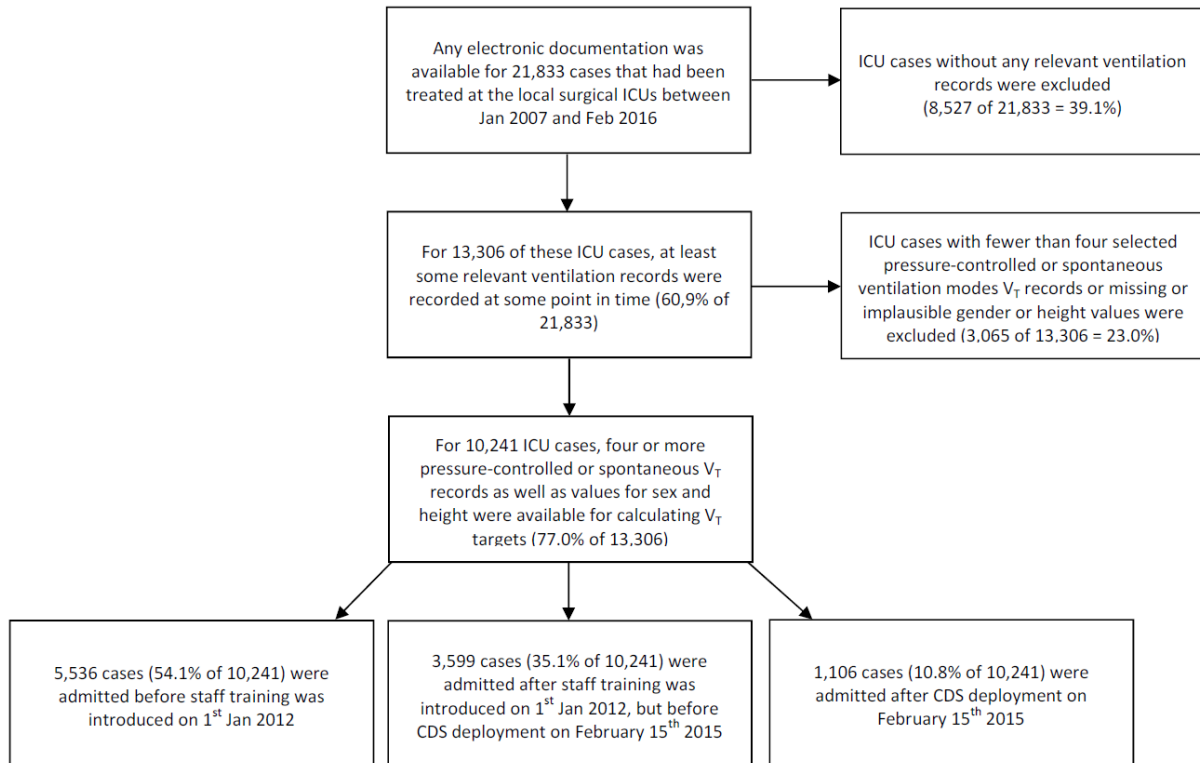


Figure 2

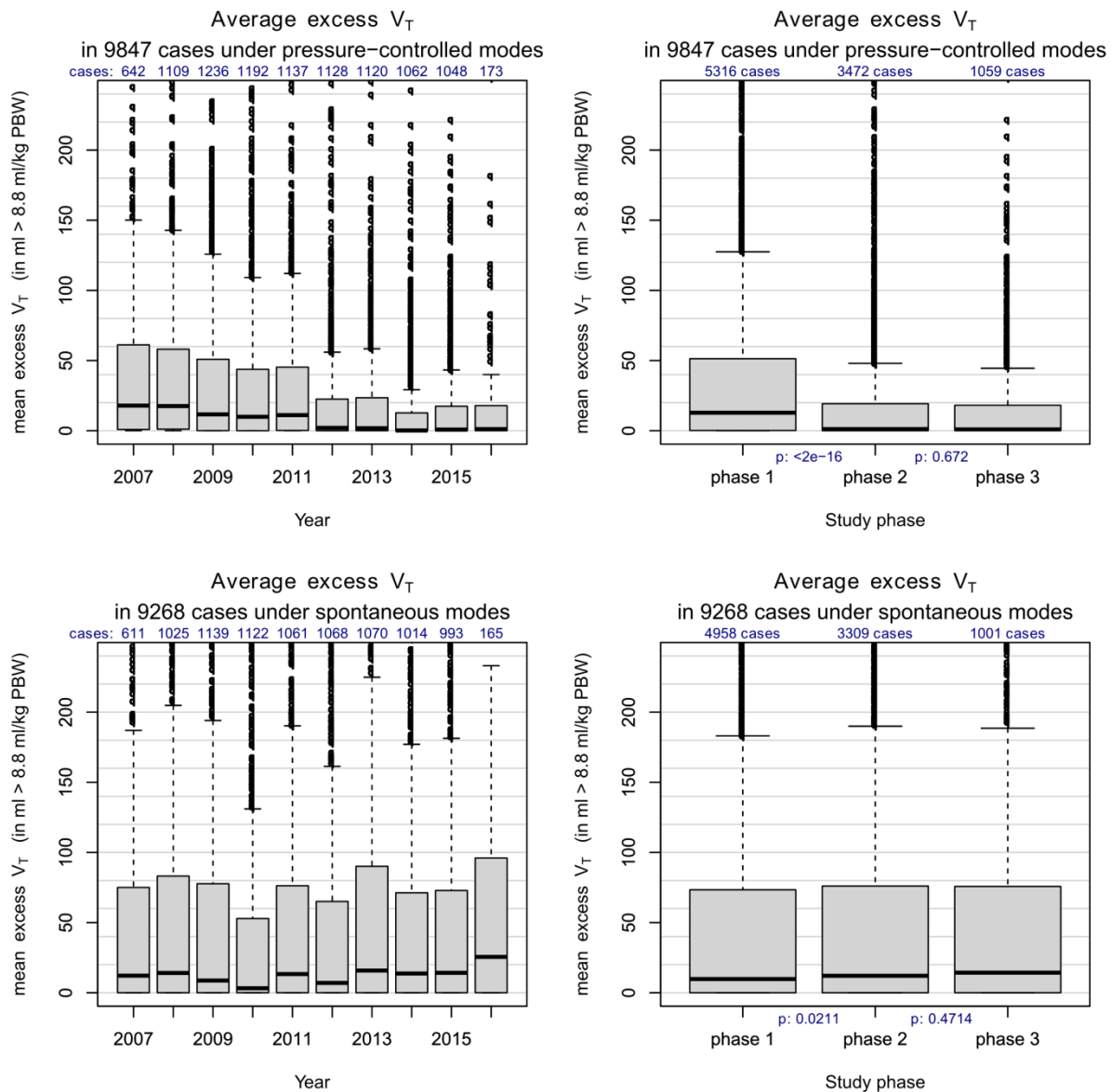


Figure 3

Highlights

- *Recommended lung-protective ventilation regimens depend on personalized settings*
- *Staff training and electronic notifications can facilitate recommendation adherence*
- *We studied their effects on tidal volumes at two surgical intensive care units*
- *After both interventions, tidal volumes moderately converged towards targets*
- *Staff training and electronic notifications can improve the precision of ventilation*

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