Would You Consider Automated Ventilation?

automated ventilation—is it about patients, or about something else?
Disclosures

• Xenios/Fresenius, Germany
• Roche Diagnostics, Netherlands
• Ferring Pharmaceuticals, Denmark
• Exvastat, UK
• Hamilton Medical AG, Switzerland
Agenda

• why
• safety
• effectiveness
• efficiency
• future
Agenda

- why
- safety
- effectiveness
- efficiency
- future

superiority & safety
non-inferiority & easiness
Agenda

• why
• safety
• effectiveness
• efficiency
• future
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
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Juffermans N *Intensive Care Med* 2022; 48:1629
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation
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Juffermans N Intensive Care Med 2022; 48:1629
QUESTION Does the use of a lower tidal volume ($V_T$) with mechanical ventilation affect important clinical outcomes in ARDS patients?

CONCLUSION Ventilation with a lower $V_T$ than is traditionally used results in decreased mortality and increases the number of days without ventilator use.

POPULATION

344 Women 516 Men

Patients with ARDS

Mean Age: 52 years

LOCATION

ICUs in the USA

VENTILATION STRATEGIES

861 patients with mild, moderate or severe ARDS

432 patients
lower $V_T$
(6 ml/kg)
[~ 400 to 500 ml]

429 patients
traditional $V_T$
(12 ml/kg)
[~1000 to 1200 ml]

(FRIMARY) OUTCOME

Hospital mortality and duration of invasive ventilation

FINDINGS

QUESTION How was ventilation managed and what were the outcomes in invasively ventilated patients with COVID-19 in the Netherlands during the first months of the outbreak?

CONCLUSION Lung-protective ventilation with low $V_T$ and low $\Delta P$ was broadly applied and prone positioning was often used; applied PEEP varied widely, despite an invariably low respiratory system compliance.

POPULATION

320 Women 802 Men
Consecutive invasive ventilated patients in the first month of the national outbreak

Median Age: 67 years

LOCATION

22 ICUs in the Netherlands

TYPE OF VENTILATORY SUPPORT

individual patient data from 1122 patients

1022 (invasively) ventilated
0 not ventilated

(PRIMARY) OUTCOME

a combination of $V_T$, PEEP, $C_{RS}$ and $\Delta P$ over the first 4 calendar days of ventilation; adjunctive treatments; VFD–28, LOS and mortality

FINDINGS

$V_T$ had an independent association with mortality (OR, 1.28 [1.00–1.64]; $P=.049$)

QUESTION Is there heterogeneity in treatment effects in patients enrolled in the ART, using a machine learning approach?

CONCLUSION Recruitment maneuvers and titrated PEEP may be harmful in ARDS patients with pneumonia or requiring vasopressor support. Driving pressure appears to modulate the association between the ART study intervention, etiology of ARDS, and mortality.

POPULATION

379 Women 631 Men

consecutive patients with moderate to severe ARDS

Mean Age: 51 years

LOCATION

120 ICUs from 9 countries

VENTILATION STRATEGIES

1010 patients with moderate or severe ARDS

501 patients titrated (high) PEEP [>15 cm H₂O] with RM

509 patients standard (low) PEEP [< 12 cm H₂O] without RM

FINDINGS

28–day mortality

QUESTION Does a mechanical ventilation strategy that is personalized to individual patients’ lung morphology improve the survival of patients with ARDS when compared with standard of care?

CONCLUSION Personalization of ventilation decreased mortality in patients with ARDS [in the posthoc analysis]; a ventilator strategy misaligned with lung morphology substantially increases mortality.

POPULATION

114 Women 286 Men

patients with ARDS for less than 12 hours

Median Age: 62 years

LOCATION

20 ICUs in France

INTERVENTION

400 patients with moderate to severe ARDS

204 standard care

V_T 6 ml/kg PBW

low PEEP

196 personalized care

non–focal

V_T 6 ml/kg PBW

high PEEP

with RM

focal

V_T 8 ml/kg PBW

low PEEP and prone positioning

(FININDINGS)

mortality at day 90; ventilator–free days, ARDS resolution; LOS in ICU; barotrauma

B Per protocol (n=360)

Time after inclusion (days)

HR 0.6, 95% CI 0.36–0.99; p=0.045

Control group (n=204)

Personalised group (n=156)

156 204

135 160

129 150

127 146

**QUESTION** Does a mechanical ventilation strategy that is personalized to individual patients' lung morphology improve the survival of patients with ARDS when compared with standard of care?

**CONCLUSION** Personalization of ventilation decreased mortality in patients with ARDS [in the posthoc analysis]; a ventilator strategy misaligned with lung morphology substantially increases mortality.

**POPULATION**

- 114 Women
- 286 Men

Patients with ARDS for less than 12 hours

Median Age: 62 years

**LOCATION**

20 ICUs in France

**INTERVENTION**

- 400 patients with moderate to severe ARDS
  - 204 standard care
    - VT 6 ml/kg PBW
    - low PEEP
  - 196 personalized care
    - focal
      - VT 8 ml/kg PBW
      - high PEEP with RM
    - non-focal
      - VT 6 ml/kg PBW
      - low PEEP and prone positioning

**FINDINGS**

**(PRIMARY) OUTCOME**

- mortality at day 90; ventilator–free days, ARDS resolution; LOS in ICU; barotrauma

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QUESTION Is ΔP an index more strongly associated with survival than $V_T$ or PEEP in patients who are not actively breathing?

CONCLUSION $\Delta P$ is the ventilation variable that best stratified risk; decreases in $\Delta P$ owing to changes in ventilator settings may be strongly associated with increased survival.

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>METHODS</th>
<th>FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>~40% Women ~60% Men</td>
<td>multilevel mediation analysis of individual patient data from 3562 patients</td>
<td></td>
</tr>
<tr>
<td>patients with ARDS included in RCTs</td>
<td></td>
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<tr>
<td>Mean Age: from 34 to 60 years</td>
<td></td>
<td></td>
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<tr>
<td>SOURCE</td>
<td>prediction model</td>
<td></td>
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<tr>
<td>9 trials worldwide</td>
<td>univariate</td>
<td></td>
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<tr>
<td></td>
<td>multivariate</td>
<td></td>
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<tr>
<td></td>
<td>mediation analysis</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>(PRIMARY) OUTCOME</td>
<td></td>
<td></td>
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<tr>
<td>60–day mortality</td>
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</tbody>
</table>

QUESTION What is the association between exposure to different intensities of mechanical ventilation over time and intensive care unit (ICU) mortality in patients with acute respiratory failure?

CONCLUSION Cumulative exposure to higher intensities of mechanical ventilation was harmful, even for short durations.

POPULATION

5141 Women 8267 Men

patients receiving ventilation for 4 hours or more

Median Age: 62 years

LOCATION

9 ICUs in Toronto, Canada

FINDINGS

<table>
<thead>
<tr>
<th>Baseline variables</th>
<th>Exposure to high driving pressure</th>
<th>Exposure to high mechanical power</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR estimate (95% CI) p-value</td>
<td>HR estimate (95% CI) p-value</td>
</tr>
<tr>
<td>PaO_{2}/FiO_{2}, mm Hg</td>
<td>0.945 (0.896-0.994) 0.026</td>
<td>0.977 (0.930-1.031) 0.38</td>
</tr>
<tr>
<td>Age, years</td>
<td>1.008 (1.048-1.156) &lt;0.0001</td>
<td>1.128 (1.080-1.182) &lt;0.0001</td>
</tr>
<tr>
<td>APACHE III score</td>
<td>1.602 (1.526-1.680) &lt;0.0001</td>
<td>1.591 (1.524-1.669) &lt;0.0001</td>
</tr>
<tr>
<td>APACHE pH</td>
<td>0.832 (0.780-0.890) &lt;0.0001</td>
<td>0.840 (0.820-0.864) &lt;0.0001</td>
</tr>
</tbody>
</table>

Time-varying variables

- Days with driving pressure ≥55 cm H\textsubscript{2}O: 1.089 (1.023-1.167) <0.0001
- Days with mechanical power ≥57 J/min: 1.069 (1.047-1.092) <0.0001

1652 (20.6%) of 7876 patients died. 64 281 daily observations were recorded. HRs were the adjusted HRs associated with a 1-SD increment in the given variable. Values higher than 1 indicate increased mortality. The values used for SDs were as follows: PaO\textsubscript{2}/FiO\textsubscript{2}, ratio 113; pH 0.11; age 17 years; and APACHE III score 29. The effects of the number of days with either driving pressure greater than or equal to 15 cm H\textsubscript{2}O or mechanical power greater than or equal to 17 J/min were estimated using Quasi-Poisson models in the joint model analysis. HR hazard ratio. CI = credible interval. PaO\textsubscript{2} = partial pressure of oxygen. FiO\textsubscript{2} = fraction of inspired oxygen. APACHE = Acute Physiology and Chronic Health Evaluation.

Table 3: Cumulative effect on HRs of exposure to high intensities of mechanical ventilation for 7876 patients with available data


courtesy by Marcus Schultz
Fig. 1 Contributions over time to the knowledge of how to apply protective ventilation

Juffermans N *Intensive Care Med* 2022; in press
Healthcare Workers

- gaps between supply and demands

Angus D. *JAMA* 2000; 284:2762
Healthcare Workers

- gaps between supply and demands
Healthcare Workers

- gaps between supply and demands
quarantine
oxygen shortages

Courtesy by Marcus Schultz
A History of Automated Ventilation

Despite years of research in mechanical ventilation many settings remained to be set by hand 
Here is when the ventilators became smarter

1. 1992  PAV+
   - PAV+ monitors flow and volume 
   - inspiratory assist in proportion to patient’s effort

2. 1998  ASV
   - automated selection of $V_t$ and RR 
   - according to the least WOB (Otis)

3. 2002  NAVA
   - monitors diaphragm activity 
   - inspiratory assist in proportion to diaphragm activity

4. 2006  SmartCare
   - automated weaning mode 
   - monitors $V_t$, RR, etCO$_2$ 
   - reduction of PS and performs SBT

5. 2016  INTELLlVENT–ASV
   - automated selection of $V_t$ and RR 
   - according to the least WOB (Otis) and FOB (Mead) 
   - monitors $V_t$, RR, etCO$_2$ and SpO$_2$ 
   - automated titrations of AMV, PEEP and FiO$_2$ 
   - reduction of AMV via reduction of PS, performs SBT
Agenda

- why
- safety
- effectiveness
- efficiency
- future
Safety

• derangement requiring immediate intervention
• (severe) adverse events
• unsafe ‘ventilation ranges’
Safety

• derangement requiring immediate intervention
• (severe) adverse events
• unsafe ‘ventilation ranges’
### Table 3. Safety of INTELLiVENT–ASV.

<table>
<thead>
<tr>
<th>Author</th>
<th>Ref.</th>
<th>Ventilation parameter</th>
<th>Not acceptable range</th>
<th>Time within not acceptable range (min)</th>
<th>Time within not acceptable range (%)</th>
<th>Incidence of episodes of derangements (n/%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lellouche et al. (2013)</td>
<td>43</td>
<td>$V_T$ (ml/kg PBW)</td>
<td>&gt; 12</td>
<td>1 ± 4 vs 15 ± 38*</td>
<td>0.5 vs 7.3*</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>etCO$_2$ (mmHg)</td>
<td>&lt; 25 or ≥ 51</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Plateau pressure (cmH$_2$O)</td>
<td>&gt; 35</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>SpO$_2$ (%)</td>
<td>&lt; 85</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bialais et al. (2016)</td>
<td>46</td>
<td>$V_T$ (ml/kg PBW)</td>
<td>&lt; 3 or &gt; 12$^{ab,c}$</td>
<td>1.3 (0.1–8.0) vs 0.8 (1.1–4.3)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>RR (breath/min)</td>
<td>&lt; 10 or &gt; 30$^a$</td>
<td>0.9 (1.4–8.5) vs 1.7 (2.7–14.1)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;10 or &gt; 35$^b$</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 83$^c$</td>
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<td></td>
<td></td>
<td>$P_{max}$ (cmH$_2$O)</td>
<td>&gt; 30$^{ab,c}$</td>
<td>6.4 (13.3–31.6) vs 0.0 (7.1–30.4)**</td>
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<tr>
<td></td>
<td></td>
<td>SpO$_2$ (%)</td>
<td>&lt; 90$^a$</td>
<td></td>
<td>0.5 (0.6–3.0) vs 0.7 (1.4–6.1)</td>
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<td></td>
<td></td>
<td></td>
<td>&lt; 83$^c$</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>etCO$_2$ (mmHg)</td>
<td>&gt; 55$^a$</td>
<td></td>
<td>0.0 (0.1–2.3) vs 0.1 (1.6–15.8)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 26 or &gt; 43$^b$</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 30 or &gt; 65$^c$</td>
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<tr>
<td>Fot et al. (2017)</td>
<td>47</td>
<td>$V_T$ (ml/kg PBW)</td>
<td>&lt; 6</td>
<td></td>
<td>3/17 vs 11/55</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&gt; 10</td>
<td>-</td>
<td>1/6 vs 5/25</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>etCO$_2$ (mmHg)</td>
<td>&lt; 25</td>
<td>-</td>
<td>5/28 vs 7/35</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RR (breath/min)</td>
<td>&gt; 45</td>
<td>-</td>
<td>6/33 vs 9/45</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SpO$_2$ (%)</td>
<td>&lt; 90</td>
<td>-</td>
<td>3/17 vs 7/35</td>
<td></td>
</tr>
<tr>
<td>Chelly et al. (2020)</td>
<td>50</td>
<td>SpO$_2$ (%)</td>
<td>&lt; 90</td>
<td>5 ± 12 vs 6 ± 11$^*$</td>
<td>30/11 vs 50/19$^*$</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 85</td>
<td>2 ± 6 vs 3 ± 8$^*$</td>
<td>69/26 vs 92/35$^*$</td>
<td></td>
</tr>
<tr>
<td>De Bie et al. (2020)</td>
<td>51</td>
<td>$V_T$ (ml/kg PBW)</td>
<td>&gt; 12</td>
<td>1.5 ± 4.7 vs 3.6 ± 8.1*</td>
<td>23,710/4.7 vs 38,929/7.3$^{*cd}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$P_{max}$ (cmH$_2$O)</td>
<td>≥ 36</td>
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<td>SpO$_2$ (%)</td>
<td>&lt; 85</td>
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</tbody>
</table>
just fine

wrong

Schultz M. Eur Resp J 2019; 54:1901588

courtesy by Marcus Schultz
Agenda

- why
- safety
- effectiveness
- efficiency
- future
**QUESTION** In patients receiving post–operative ventilation after cardiac surgery, does INTELLiVENT–ASV improve the quality of breathing compared with conventional ventilation?

**CONCLUSION** Fully automated ventilation in patients after cardiac surgery optimized lung–protective ventilation during postoperative ventilation, with fewer episodes of severe hypoxaemia and an accelerated resumption of spontaneous breathing.

**POPULATION**

- 67 Women
- 153 Men

Patients after uncomplicated cardiac surgery

**LOCATION**

1 ICU in the Netherlands

**INTERVENTION**

- 220 patients after surgery
- 111 conventional ventilation
- 109 automated ventilation

**FINDINGS**

**(PRIMARY) OUTCOME**

- Proportion of breath within predefined optimal, acceptable, and critical ranges ($V_T$, $P_{max}$, $SpO_2$ and $etCO_2$);
- Severe hypoxaemia ($SpO_2 < 85\%$) and resumption of spontaneous breathing.

**REFERENCE**

POSITiVE–investigators. Fully automated postoperative ventilation in cardiac surgery patients: a randomized clinical trial. [BJA 2021; 125:739; doi: 10.1016/j.bja.2020.06.037]
QUESTION Is the amount of mechanical power of ventilation (MP) under adaptive support ventilation (ASV) different from that under nonautomated pressure–controlled ventilation?

CONCLUSION This study suggests ASV may have benefits compared with pressure–controlled ventilation with respect to the MP transferred from the ventilator to the respiratory system in passive invasively ventilated critically ill patients.

POPULATION

7 Women  15 Men

patients expected to need invasive ventilation for the next 24 hours

Median Age: 67 years

LOCATION

1 ICUs in The Netherlands

**QUESTION** In COVID–19 patients with ARDS, does INTELLiVENT–ASV reduce the driving pressure and mechanical power of ventilation compared with conventional ventilation?

**CONCLUSION** INTELLiVENT–ASV reduces the intensity of ventilation in COVID–19 patients with ARDS.

**POPULATION**

12 Women  39 Men

COVID–19 with moderate to severe ARDS

Median Age: 63 years

**LOCATION**

2 ICUs in the Netherlands

**INTERVENTION**

51 patients intubated in the ICU for acute hypoxemia

conventional ventilation → automated ventilation
crossover

**(PRIMARY) OUTCOME**

ΔP and MP before and after converting from conventional ventilation to INTELLiVENT–ASV

QUESTION In COVID–19 patients with ARDS, does INTELLiVENT–ASV reduce the driving pressure and mechanical power of ventilation compared with conventional ventilation?

CONCLUSION INTELLiVENT–ASV reduces the intensity of ventilation in COVID–19 patients with ARDS.

POPULATION

12 Women 39 Men

COVID–19 with moderate to severe ARDS

Median Age: 63 years

LOCATION

2 ICUs in the Netherlands

QUESTION What is the effect of automated closed–loop oxygen control, compared to automated ventilation with manual oxygen titrations, on time spent in predefined pulse oximetry (SpO₂) zones in pediatric critically ill patients?

CONCLUSION In this randomized crossover trial in pediatric critically ill patients under invasive ventilation with ASV, the percentage of time spent within in optimal SpO₂ zones increased with the use of closed–loop oxygen control.

POPULATION

37 Pediatric Patients

children with or without ARDS under invasive ventilation

Median Age: 1 year

LOCATION

1 ICU in Turkey

INTERVENTION

37 patients under ASV for acute hypoxemia

2 hours manual or automated FiO₂ control

crossover

2 hours automated or manual FiO₂ control

(PRIMARY) OUTCOME

FiO₂ settings and SpO₂ readings

RESULTS

MANUAL % of time

AUTOMATED % of time

0 20 40 60 80 100

Time, %

suboptimally low

acceptably low

optimal

unacceptably high

acceptably high

low PEEP group

high PEEP group

courtesy by Marcus Schultz

QUESTION What is the efficacy of a closed–loop oxygen control in critically ill patients with moderate to severe acute hypoxemic respiratory failure (AHRF) treated with high flow nasal oxygen (HFNO).

CONCLUSION Closed–loop oxygen control improves oxygen administration in patients with moderate-to-severe AHRF treated with HFNO, increasing the percentage of time in the optimal oxygenation range and decreasing the workload of healthcare personnel.

POPULATION

45 patients under HFNO

patients with moderate to severe ARF, including patients with COVID-19

Median Age: 49 year

LOCATION

1 ICU in Spain

INTERVENTION

45 patients under HFNO

4 hours manual or automated FiO₂ control

crossover

4 hours automated or manual FiO₂ control

(PRIMARY) OUTCOME

percentage of time spent in the individualized optimal SpO₂ ranges

RESULTS

Roca O. Closed–loop oxygen control improves oxygen therapy in acute hypoxemic respiratory failure patients under high flow nasal oxygen (HILOOP): a randomized cross-over study. [Crit Care 2022; 26:108; doi10.1186/s13054-022-03970-w] 

courtesy by Marcus Schultz
**QUESTION** What is the effect of HFNO with closed–loop control of the fraction of inspired oxygen (FiO₂), compared to HFNO with manual titrations of the FiO₂, on time spent in predefined pulse oximetry (SpO₂) zones in pediatric critically ill patients?

**CONCLUSION** In this randomized crossover trial in pediatric critically ill patients under HFNO, the percentage of time spent within in optimal SpO₂ zones increased with the use of closed–loop FiO₂ control.

**POPULATION**

23 Pediatric Patients

children with acute hypoxemic respiratory failure under HFNO

Median Age: 1 year

**LOCATION**

3 ICUs in Turkey

**INTERVENTION**

23 patients under HFNO for acute hypoxemia

manual or automated FiO₂ control

crossover

automated or manual FiO₂ control

**RESULTS**

FiO₂ settings and SpO₂ readings; alarms and manual adjustments

**(PRIMARY) OUTCOME**

unacceptably low

optimal

suboptimally low

suboptimally high

unacceptably high

**courtesy by Marcus Schultz**

Agenda

- why
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Agenda

• why
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Challenges

• reduction in workloads?
  • what is workload
  • how to measure workload
  • cost–effectiveness?
  • translation in better … what?
Future

• benefits of automated ventilation are ‘safety’ and ‘effectiveness’
• automated ventilation is non–inferior to conventional ventilation with regard to outcomes
• workloads, workloads, workloads, workloads, workloads, workloads, workloads, workloads, workloads
• scarcities, scarcities, scarcities, scarcities, scarcities, scarcities, scarcities, scarcities
Take Home Messages

• do no longer expect studies about superiority with respect to mortality
• expect studies about workloads & scarcities