Master Class
A systematic review of the effectiveness of protocolized weaning

Dr Bronagh Blackwood PhD RGN
What I’m going to talk about

1. Background (why I became interested in protocolized weaning; reasons why it was important to do the review)

2. What I did to gather the evidence (the steps in systematic reviewing)

3. More importantly, what I found & how it affects your practice (the meta-analysis & interpretation)
Weaning

- Why is weaning important?
- How are patients weaned?
- What’s the best most effective way?
- What’s the best protocol?
- Is weaning by protocol any better than usual practice?
Why I became interested in protocolized weaning

Protocol Weaning of Mechanical Ventilation in Medical and Surgical Patients by Respiratory Care Practitioners and Nurses: Effect on Weaning Time and Incidence of Ventilator-Associated Pneumonia

Gregory P. Marelich, Susan Murin, Felix Battistella, John Inciardi, Terry Vierra and Marc Roby

Chest 2000;118:459-467
DOI 10.1378/chest.118.2.459

The duration of mechanical ventilation for patients was decreased from a median of 124 h for the control group to 68 h in the protocol group (p = 0.0001)

Can protocolised-weaning developed in the United States transfer to the United Kingdom context: a discussion

Bronagh Blackwood

An evaluation of protocolised weaning on the duration of mechanical ventilation

B. Blackwood,¹ J. Wilson-Barnett,² C. C. Patterson,³ T. J. Trinder⁴ and G. G. Lavery⁵

Table 4 Comparison of outcomes between Phases in the intervention and reference units. Values are median number of hours (interquartile range) or ratio of geometric means (95% CI).

<table>
<thead>
<tr>
<th></th>
<th>Phase I</th>
<th>Phase II</th>
<th>p value</th>
<th>Ratio of geometric means (95% CI) (after adjustment for confounders*)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention unit</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Duration of mechanical ventilation</td>
<td>98 (23, 236)</td>
<td>177 (49, 326)</td>
<td>0.001</td>
<td>1.22 (0.95, 1.57)</td>
<td>0.11</td>
</tr>
<tr>
<td>Duration of intubation</td>
<td>107 (23, 233)</td>
<td>195 (60, 337)</td>
<td>&lt; 0.001</td>
<td>1.27 (0.99, 1.63)</td>
<td>0.06</td>
</tr>
<tr>
<td>ICU stay</td>
<td>150 (49, 283)</td>
<td>226 (82, 406)</td>
<td>&lt; 0.001</td>
<td>1.41 (1.14, 1.74)</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Reference unit</strong></td>
<td></td>
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<tr>
<td>Duration of mechanical ventilation</td>
<td>132 (39, 232)</td>
<td>154 (65, 270)</td>
<td>0.20</td>
<td>1.23 (0.89, 1.71)</td>
<td>0.21</td>
</tr>
<tr>
<td>Duration of intubation</td>
<td>159 (58, 267)</td>
<td>196 (92, 331)</td>
<td>0.06</td>
<td>1.30 (0.96, 1.76)</td>
<td>0.10</td>
</tr>
<tr>
<td>ICU stay</td>
<td>212 (108, 385)</td>
<td>249 (125, 424)</td>
<td>0.53</td>
<td>1.06 (0.82, 1.36)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

*Adjusted for admission APACHE II score category and patient’s diagnostic category.
Are weaning protocols effective?

**Significant findings**
- 1995 Wood
- 1996 Ely
- 1996 Saura
- 1997 Kollef
- 1998 Horst
- 2000 Marelich
- 2001 Scheinhorn
- 2003 Grap

**Non-significant findings**
- 1993 Strickland
- 1998 Burns
- 1998a Kollef
- 1998b Kollef
- 2002 Duane
- 2006 Blackwood
Archie Cochrane

“... a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, ... of all relevant randomised controlled trials.”

Critical summary came to be known as a systematic review.

Subsequently, the Cochrane Collaboration was established to prepare, maintain and promote the accessibility of systematic reviews of the effects of health care interventions.
Systematic Review – 4 key points

- Good, focused question
- Comprehensive literature/data search with unbiased selection
- Critical appraisal of literature/data
- Description & synthesis of literature and/or data
Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients (Review)

Blackwood B, Alderdice F, Burns KEA, Cardwell CR, Lavery G, O’Halloran P
Architecture of a good focused question: PICO format

P - What is the population or what problem is being addressed?

I - What is the intervention or exposure?

C – What is the comparator?

O - What is the outcome or endpoint?

Adapted from Madhukar Pai, University of California
Focused question

- Does protocolized weaning in comparison to non-protocolized weaning reduce the duration of mechanical ventilation in critically ill adults?

- Inclusion criteria: RCTs; protocolized weaning (automated or professional led); standard practice; adults in ICU
Transparent search strategy

- **Sources:**
  - Systematic review databases
  - Electronic databases
  - Trial registers
  - Conference proceedings
  - Theses

- **Restrictions (time? language?)**
- **Reliability in selecting, data extracting & quality assessment (usually 2 authors)**
Quality Assessment

- Not all published research is good
- Poor quality trials increase the risk of bias
- Leads to less confidence in the evidence
High risk of bias if...

- Randomisation process is predictable:
  - Sequence generation is known
  - Allocation to groups not concealed
- Different behaviours in groups as a result of patient, personnel or assessor knowing group allocation
- Incomplete outcome data
Description & synthesis

- Describe the studies included (& those excluded with reasons)

- Clinicians want to see similarities & differences
  - Countries, settings (ICUs), patient types
  - Protocol methods, weaning criteria, outcomes recorded

- Describe/summarise the quality

- Synthesise data in a meta-analysis (if possible).
11 Randomized Controlled Trials
(N= 1971 participants)

USA
- Ely 1996, medical & coronary ICU (n=300)
- Kollef 1997, medical & surgical ICUs (n=357)
- Krishnan 2004, medical ICU (n=299)
- Marelich 2000, medical & surgical ICUs (n=335)
- Namen 2001, neurosurgical ICU (100)
- Strickland 1993, medical & surgical (n=15)*

Brazil
- Piotto 2008, coronary care unit (n=36)

Germany
- Stahl 2009, surgical ICU (n=60)*

Italy
- Simeone 2002, cardiac surgical ICU (n=49)

Australia
- Rose 2008, mixed medical, surgical & trauma (102)*

* Automated weaning protocols
### Study quality - risk of bias

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<tr>
<td>Ely 1996</td>
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<td>+</td>
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<td>Kollef 1997</td>
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<td>+</td>
<td>+</td>
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<td>+</td>
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<td>Krishnan 2004</td>
<td>-</td>
<td>-</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Marelich 2000</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>Navalesi 2008</td>
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<td>+</td>
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<td>+</td>
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<td>Piotto 2008</td>
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<td>-</td>
<td>-</td>
<td>+</td>
<td>?</td>
<td>?</td>
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<td>Rose 2008</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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<td>Simeone 2002</td>
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<td>+</td>
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<td>?</td>
<td>?</td>
<td>?</td>
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<td>Stahl 2009</td>
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<td>+</td>
<td>?</td>
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<tr>
<td>Strickland 1993</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tbody>
</table>
Results…

In comparison with standard care.

- Total duration of mechanical ventilation in the protocolized weaning group reduced by 25% (95% CI 9 – 39%, p=0.06)
- Weaning duration reduced by 78% (95% CI 31-93%, p=0.009)
- ICU length of stay reduced by 10% (95% CI 2-19%, p=0.02)
3.1 Total duration of MV [hours]

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean [hours]</th>
<th>SD [hours]</th>
<th>Total Mean [hours]</th>
<th>SD [hours]</th>
<th>Total Mean [hours]</th>
<th>SD [hours]</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Random, 95% CI [hours]</th>
<th>Mean Difference IV, Random, 95% CI [hours]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ely 1996</td>
<td>151.2</td>
<td>175.2</td>
<td>149</td>
<td>211.2</td>
<td>261.6</td>
<td>151</td>
<td>7.5%</td>
<td>-50.00</td>
<td>[-110.32, -9.68]</td>
<td></td>
</tr>
<tr>
<td>Kollef 1997</td>
<td>69.4</td>
<td>123.7</td>
<td>179</td>
<td>102</td>
<td>169.1</td>
<td>178</td>
<td>13.3%</td>
<td>-32.60</td>
<td>[-63.35, -1.85]</td>
<td></td>
</tr>
<tr>
<td>Krishnan 2004</td>
<td>70.4</td>
<td>103</td>
<td>115</td>
<td>68</td>
<td>105.3</td>
<td>109</td>
<td>14.8%</td>
<td>-7.60</td>
<td>[-34.90, 19.70]</td>
<td></td>
</tr>
<tr>
<td>Marelich 2000</td>
<td>68</td>
<td>97</td>
<td>166</td>
<td>124</td>
<td>207</td>
<td>169</td>
<td>11.9%</td>
<td>-56.00</td>
<td>[-90.52, -21.48]</td>
<td></td>
</tr>
<tr>
<td>Namer 2001</td>
<td>144</td>
<td>124.45</td>
<td>48</td>
<td>144</td>
<td>195.56</td>
<td>51</td>
<td>5.2%</td>
<td>0.00</td>
<td>[-63.99, 83.99]</td>
<td></td>
</tr>
<tr>
<td>Narales 2008</td>
<td>120</td>
<td>134.45</td>
<td>48</td>
<td>120</td>
<td>195.56</td>
<td>51</td>
<td>14.5%</td>
<td>0.00</td>
<td>[-27.97, 27.97]</td>
<td></td>
</tr>
<tr>
<td>Piotto 2008</td>
<td>189.25</td>
<td>463.55</td>
<td>16</td>
<td>127.48</td>
<td>337.37</td>
<td>18</td>
<td>4.4%</td>
<td>61.77</td>
<td>[203.09, 326.63]</td>
<td></td>
</tr>
<tr>
<td>Rose 2008</td>
<td>119</td>
<td>174.89</td>
<td>51</td>
<td>129</td>
<td>197.07</td>
<td>51</td>
<td>4.3%</td>
<td>-10.00</td>
<td>[82.31, 62.31]</td>
<td></td>
</tr>
<tr>
<td>Simeone 2002</td>
<td>6.54</td>
<td>3.78</td>
<td>24</td>
<td>8.58</td>
<td>3.45</td>
<td>25</td>
<td>24.8%</td>
<td>-2.04</td>
<td>[-4.07, -0.01]</td>
<td></td>
</tr>
<tr>
<td>Stahl 2009</td>
<td>135.6</td>
<td>122.1</td>
<td>26</td>
<td>199.44</td>
<td>172.3</td>
<td>26</td>
<td>3.5%</td>
<td>-63.84</td>
<td>[-145.01, 17.33]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>842</td>
<td>931</td>
<td>-19.50 [-35.91, -3.10]</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 231.11; \chi^2 = 20.75, \text{df} = 8 (P = 0.01); \rho = 57\%$

Test for overall effect $Z = 2.33 \ (P = 0.02)$
3.2 Weaning duration [hours]

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Mean Difference IV, Random, 95% CI [hours]</th>
<th>Mean Difference IV, Random, 95% CI [hours]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ely 1996</td>
<td>108</td>
<td>144</td>
<td>-36.00 [-110.75, 38.75]</td>
<td></td>
</tr>
<tr>
<td>Marelich 2000</td>
<td>38</td>
<td>97</td>
<td>-59.00 [-81.82, -36.18]</td>
<td></td>
</tr>
<tr>
<td>Pictto 2008</td>
<td>2.1</td>
<td>69.5</td>
<td>-67.40 [-97.59, -37.21]</td>
<td></td>
</tr>
<tr>
<td>Rose 2008</td>
<td>69.89</td>
<td>98.08</td>
<td>-28.19 [-74.96, 18.58]</td>
<td></td>
</tr>
<tr>
<td>Stehl 2009</td>
<td>15.4</td>
<td>55.92</td>
<td>-40.52 [-92.04, 11.07]</td>
<td></td>
</tr>
<tr>
<td>Strickland 1993</td>
<td>18.7</td>
<td>25.6</td>
<td>-6.90 [-15.61, 2.01]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>421</strong></td>
<td><strong>285</strong></td>
<td><strong>-39.41 [-68.74, -10.09]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 952.78; Chi² = 29.77, df = 5 (P < 0.0001); I² = 83%
Test for overall effect: Z = 2.63 (P = 0.008)
### 3.3 ICU length of stay [hours]

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean [hours]</th>
<th>SD [hours]</th>
<th>Total</th>
<th>Control Mean [hours]</th>
<th>SD [hours]</th>
<th>Total</th>
<th>Weight</th>
<th>IV, Fixed, 95% CI [hours]</th>
<th>Mean Difference IV, Fixed, 95% CI [hours]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elv 1996</td>
<td>192</td>
<td>248.88</td>
<td>148</td>
<td>216</td>
<td>10.9</td>
<td>151</td>
<td>9.1%</td>
<td>-24.00 [-64.00, 16.00]</td>
<td></td>
</tr>
<tr>
<td>Krishnan 2004</td>
<td>115</td>
<td>209.37</td>
<td>154</td>
<td>146</td>
<td>155.56</td>
<td>145</td>
<td>8.4%</td>
<td>-31.00 [-72.65, 10.65]</td>
<td></td>
</tr>
<tr>
<td>Namens 2001</td>
<td>360</td>
<td>160</td>
<td>49</td>
<td>336</td>
<td>266.67</td>
<td>51</td>
<td>2.0%</td>
<td>24.00 [-61.81, 109.81]</td>
<td></td>
</tr>
<tr>
<td>Navalesi 2008</td>
<td>154.4</td>
<td>172.8</td>
<td>165</td>
<td>211.2</td>
<td>175.2</td>
<td>153</td>
<td>9.9%</td>
<td>-16.80 [-55.09, 21.49]</td>
<td></td>
</tr>
<tr>
<td>Platto 2008</td>
<td>554.4</td>
<td>458.2</td>
<td>18</td>
<td>564</td>
<td>373.4</td>
<td>18</td>
<td>0.2%</td>
<td>-29.00 [-282.66, 263.46]</td>
<td></td>
</tr>
<tr>
<td>Rose 2006 (1)</td>
<td>205.97</td>
<td>157.17</td>
<td>51</td>
<td>243.73</td>
<td>218.57</td>
<td>51</td>
<td>2.7%</td>
<td>-38.36 [-112.25, 35.53]</td>
<td></td>
</tr>
<tr>
<td>Simeone 2002</td>
<td>29</td>
<td>15.8</td>
<td>24</td>
<td>46.1</td>
<td>33.9</td>
<td>25</td>
<td>67.3%</td>
<td>-17.10 [-31.82, -2.38]</td>
<td></td>
</tr>
<tr>
<td>Stahl 2009</td>
<td>522.72</td>
<td>352.2</td>
<td>26</td>
<td>471.8</td>
<td>338.86</td>
<td>26</td>
<td>0.4%</td>
<td>51.12 [-138.74, 238.98]</td>
<td></td>
</tr>
</tbody>
</table>

| Total (95% CI)    | 636                       |          | 620 100.0% | -18.32 [-30.40, -6.25] | 

Heterogeneity: Chi² = 2.21, df = 7 (P = 0.95); I² = 0%
Test for overall effect: Z = 2.98 (P = 0.003)
Strengths of the review

- 1st systematic review & meta-analysis of RCT in protocolized weaning
- Trials had good methodological quality
- Considerable variability in results limits generalisation to all ICUs
- Indicates that overall the quality of evidence for using weaning protocols is low
So what might have caused the heterogeneity?

- Differences may be due to:
  - **contextual factors** (differences in patient populations and usual practice within units) or
  - **intervention factors** (differences in determining readiness to wean; weaning methods; and parameters used in weaning protocols).
What does it mean for practice?

- The use of protocols in weaning can reduce the duration of mechanical ventilation, weaning duration & ICU stay & mechanical ventilation time.
- Protocolized weaning is safe and just as beneficial as standard practice.
- Where standard practice is already of high quality, weaning protocols will not bring further benefits.
Questions that remain unanswered...

- Are certain protocols better in certain populations? (children; post-op patients)
- What factors impact on the use of weaning protocols in critically ill adults and children (a qualitative evidence synthesis)
- How effective are automated weaning systems for reducing duration of mechanical ventilation in adults & children?
- What is known about weaning management and outcomes of prolonged mechanical ventilation in adults and children?
Thank You

Questions???

Contact details
b.blackwood@qub.ac.uk