Prognosis in Prolonged Mechanical Ventilation: Role of Prognostic Models

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Disclosures

- Grant Funding
  - NHLBI, NINR

- Consultant
  - CMS, RTI
Role of Prognostic Models

- Standardize illness severity for outcomes studies
- Benchmarking for quality control
- Aid decision making?
  - Resource allocation
    - MELD score
    - Lung allocation score
  - End-of-life care
Prognostic Models-- Clinical Application

- Physicians should understand origins, strengths and limitations
  - Simplifications of complex systems
  - Derived from large groups, not specific to individual patients
- Can be useful to guide assessments
- Should not be dominant or exclusive consideration
- Information should be interpreted in context of individual patient values

Projected Growth of Prolonged Acute MV

# Outcomes of PMV

<table>
<thead>
<tr>
<th>Study</th>
<th>Combes</th>
<th>Carson</th>
<th>Cox</th>
<th>Engoren</th>
<th>Kahn</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>347</td>
<td>200</td>
<td>114</td>
<td>267</td>
<td>347</td>
</tr>
<tr>
<td>Age</td>
<td>63-67</td>
<td>58</td>
<td>66</td>
<td>66</td>
<td>64-71</td>
</tr>
<tr>
<td>Hospital</td>
<td>--</td>
<td>51</td>
<td>39</td>
<td>29</td>
<td>28-37</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>--</td>
<td>51</td>
<td>39</td>
<td>29</td>
<td>28-37</td>
</tr>
<tr>
<td>Survived</td>
<td>67%</td>
<td>59%</td>
<td>69%</td>
<td>80%</td>
<td>78%</td>
</tr>
<tr>
<td>Hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharged</td>
<td>--</td>
<td>11%</td>
<td>4%</td>
<td>7%</td>
<td>--</td>
</tr>
<tr>
<td>Home</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alive at 12</td>
<td>32%</td>
<td>48%</td>
<td>42%</td>
<td>52%</td>
<td>50%</td>
</tr>
<tr>
<td>months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 1. Trajectories of care for patients in the prolonged mechanical ventilation cohort over the first year after discharge.

Initial hospitalization (n = 126)
- Residing at 1 year: 1
- Transition to inpatient hospice: 3 *
- Died: 23

99 patients

3 patients
- Alive at 1 y: 3

Other hospital (n = 3)
- Total patients: 3
- Residing at 1 y: 0
- Died: 0

36 patients
- Alive at 1 y: 19

Long-term acute-care facility (n = 43)
- Total patients: 38
- Residing at 1 y: 0
- Died: 6 *

17 patients
- Alive at 1 y: 13

Skilled nursing facility (n = 63) *
- Total patients: 36
- Residing at 1 y: 10
- Died: 6 *

23 patients
- Alive at 1 y: 22

Inpatient rehabilitation facility (n = 54)
- Total patients: 28
- Residing at 1 y: 1
- Died: 0

20 patients
- Alive at 1 y: 13

Home (n = 136)
- Total patients: 71
- Residing at 1 y: 58
- Independent: 11
- Dependent: 47
- Died: 4 *

Hospital readmission (n = 150)
- Total patients: 68
- Died: 13 *

### Informational Needs in CCI

<table>
<thead>
<tr>
<th>Information Topic</th>
<th>Important (%)</th>
<th>Received Information (%)</th>
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</thead>
<tbody>
<tr>
<td>Risk of Hospital Death</td>
<td>89</td>
<td>64</td>
</tr>
<tr>
<td>Risk of Death by One Year</td>
<td>77</td>
<td>7</td>
</tr>
<tr>
<td>Expected Functional Status</td>
<td>99</td>
<td>20</td>
</tr>
<tr>
<td>Alternatives to Life Support</td>
<td>98</td>
<td>17</td>
</tr>
</tbody>
</table>

## Discordance

<table>
<thead>
<tr>
<th>High Expectations For:</th>
<th>Surrogates (%)</th>
<th>Physicians (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-year Survival</td>
<td>93</td>
<td>43</td>
</tr>
<tr>
<td>Functional Status</td>
<td>71</td>
<td>6</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>83</td>
<td>4</td>
</tr>
</tbody>
</table>

Concordance: $\kappa = 0.08$

Figure 2. Development of a Clinical Decision Rule

Step 1. Derivation
Identification of factors with predictive power

Step 2. Validation
Evidence of reproducible accuracy
- Narrow Validation
  Application of rule in a similar clinical setting and population as in Step 1

- Broad Validation
  Application of rule in multiple clinical settings with varying prevalence and outcomes of disease

Step 3. Impact Analysis
Evidence that rule changes physician behavior and improves patient outcomes and/or reduces costs

Level of Evidence

4 3 2 1
## PMV Mortality Risk Score

Single hospital, 200 patient development, 100 patient validation sets

<table>
<thead>
<tr>
<th>Factor</th>
<th>Points</th>
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<tbody>
<tr>
<td>Age $\geq 50$</td>
<td>1 point</td>
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<tr>
<td>Pressors</td>
<td>1 point</td>
</tr>
<tr>
<td>Platelets $\leq 150$</td>
<td>1 point</td>
</tr>
<tr>
<td>Dialysis on Day 21</td>
<td>1 point</td>
</tr>
</tbody>
</table>

Carson et al. CCM 2008; 36:2061
Survival by ProVent Score

Kaplan-Meier survival estimates, by Risk

Carson et al. CCM 2008; 36:2061
ProVent Model: External Validation

- 491 patients from 5 tertiary care centers
- Required $\geq 14$ of MV in 2005
  - Mean admission APACHE III = 80
  - Median duration MV 22 days (17-32)
  - Hospital Mortality 29%
  - 1-year Mortality 45%
- 260 patients required $\geq 21$ days MV
Validation Day 21 Model

<table>
<thead>
<tr>
<th>Effect</th>
<th>Odds Ratio Estimates</th>
<th>95% Wald Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effect</strong></td>
<td><strong>Point Estimate</strong></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.044</td>
<td>1.025</td>
</tr>
<tr>
<td>Platelet count</td>
<td>0.996</td>
<td>0.994</td>
</tr>
<tr>
<td>Vasopressors</td>
<td>2.955</td>
<td>1.032</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>2.522</td>
<td>1.003</td>
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</table>

Area under ROC curve (AUC) = 0.79
Calibration – Day 21 Model

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>Observed</th>
<th>Expected</th>
<th>Observed</th>
<th>Expected</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>26</td>
<td>1</td>
<td>1.80</td>
<td>25</td>
<td>24.20</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>3</td>
<td>3.91</td>
<td>23</td>
<td>22.09</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>8</td>
<td>6.50</td>
<td>18</td>
<td>19.50</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>11</td>
<td>9.37</td>
<td>15</td>
<td>16.63</td>
</tr>
<tr>
<td>5</td>
<td>26</td>
<td>11</td>
<td>11.54</td>
<td>15</td>
<td>14.46</td>
</tr>
<tr>
<td>6</td>
<td>26</td>
<td>15</td>
<td>13.53</td>
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<td>12.47</td>
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<tr>
<td>7</td>
<td>26</td>
<td>16</td>
<td>15.74</td>
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<td>8</td>
<td>26</td>
<td>16</td>
<td>17.72</td>
<td>10</td>
<td>8.28</td>
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<td>9</td>
<td>26</td>
<td>18</td>
<td>19.89</td>
<td>8</td>
<td>6.11</td>
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<td>10</td>
<td>26</td>
<td>24</td>
<td>23.01</td>
<td>2</td>
<td>2.99</td>
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</tbody>
</table>

p=0.88

Crit Care Med 2011; In press
Day 14 Model Development

Hemodialysis: 10%
Platelets: Mean 316 K
Vasopressors: 12%
Age: Mean 55
Trauma: 24%
PEEP, WBC, glucose, gender

Cross Validation: 60% sample x 50; AUC 0.80 ± 0.02

Proc Am Thor Soc 2011
## Calibration – 14 Day Model

<table>
<thead>
<tr>
<th>Group</th>
<th>Total</th>
<th>Dead 1 yr</th>
<th>Alive 1 yr</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td>Observed</td>
<td>Expected</td>
</tr>
<tr>
<td>1</td>
<td>49</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>2</td>
<td>49</td>
<td>6</td>
<td>6.3</td>
</tr>
<tr>
<td>3</td>
<td>49</td>
<td>14</td>
<td>11.6</td>
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<tr>
<td>4</td>
<td>49</td>
<td>13</td>
<td>16.5</td>
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<tr>
<td>5</td>
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<td>23</td>
<td>20.2</td>
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<td>23.9</td>
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<tr>
<td>7</td>
<td>49</td>
<td>26</td>
<td>27.7</td>
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<tr>
<td>8</td>
<td>49</td>
<td>32</td>
<td>32.0</td>
</tr>
<tr>
<td>9</td>
<td>49</td>
<td>34</td>
<td>36.3</td>
</tr>
<tr>
<td>10</td>
<td>50</td>
<td>45</td>
<td>44.2</td>
</tr>
</tbody>
</table>

p=0.89
ProVent-14 Score

Age $\geq 65$: 2 points
Age 50 – 64: 1 point
Platelets $\leq 100$: 1 point
Vasopressors: 1 point
Hemodialysis: 1 point
Non-trauma: 1 point
ProVent-14: External Validation

ARDSNet FACTT cohort

342 of 1000 patients MV ≥ 14 days

- Mean age 53 years old
- 12% Trauma
- 14% receiving vasopressors
- 14% required hemodialysis
- 1-year mortality 59% (45% in ProVent cohort)

ProVent -14 Score – FACTT Cohort

ProVent Cohort
AUC = 0.80

FACTT Cohort
AUC = 0.78

GoF $p = 0.06$
Survival by ProVent Score

Kaplan-Meier survival estimates, by Risk

- 39% independent
- 18% independent
- None independent

Carson et al. CCM 2008; 36:2061
Figure 2. Development of a Clinical Decision Rule

Step 1. Derivation
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Step 3. Impact Analysis
Evidence that rule changes physician behavior and improves patient outcomes and/or reduces costs

Level of Evidence
4 3 2 1

McGinn et al. JAMA 2000;284:79
Prognostication

Foreseeing

Foretelling
Informing Decisions in Chronic Critical Illness: An RCT

Study Overview

ClinicalTrials.gov  NCT01230099
Conceptual Model

- Proactive, Protocol-Based Family Meetings

- Information Support
  - Framework for Goal-Directed Decision-Making About Treatment of Chronic Critical Illness

- Printed Informational Aid

- Informed/Timely Establishment of Treatment Goals

- ICU/Family Decisions in Context of Treatment Goals

- Improved Outcomes
Support and Information Team Intervention for PMV Patients

Day 7 - 10 of Ventilation Families

Structured Meeting of SIT Clinicians With Family Information Brochure

Second Meeting

12-14 Days after Randomization

Interview Families for Study Outcomes

Usual Care Information Brochure

90 Days
Decision Aid for PMV

- Clinical information about PMV
- Individualized prognostic information
  - ProVent-14
- Reviews treatment options
- Elicits surrogates’ understanding
- Provides guidance in deliberation and communication

Chris Cox and ProVent Study Team
Decision-Making: Goals of Treatment

1. Comfort
   - Provide medications to relieve pain & anxiety
   - Death often occurs during the hospitalization
   - Avoid procedures like: tracheostomy placement, feeding tube placement, more life support like dialysis

2. Aim for Survival but Avoid Prolonged Treatment and Discomfort
   - Try to remove breathing tube successfully
   - Usually avoids: tracheostomy, feeding tube, more life support like dialysis

3. Survival at All Cost
   - Try to remove breathing tube successfully
   - May require: tracheostomy placement, feeding tube placement

Figure 5: Decision Support Tool Conceptual Model
Decision Aid - Pilot Study

Decision Aid vs Usual Care
Before/After design
30 Surrogates, Duke and UNC
-10 Control, 20 Intervention
30 physicians, 20 nurses

ProVent Study Investigators

Chris Cox
Ivor Douglas
Terri Hough
Jeremy Kahn
Gordon Rubenfeld
Eric Seeley
Doug White
Laura Hanson
Judy Nelson
Kevin Fischer
Joyce Lanier
Joe Govert
Tim Carey
Summary

- Prognostic models are useful for standardization of illness severity for research and quality assessments.
- Models can be useful in clinical practice to support decision making but should only be used in context of a given patient’s condition.
- The ProVent model is a simple clinical prediction rule that can identify patients with PMV who are at high risk of death.
Prognostic Models-- Clinical Application

- Physicians should understand origins, strengths and limitations
  - Simplifications of complex systems
  - Derived from large groups, not specific to individual patients
- Can be useful to guide assessments
- Should not be dominant or exclusive consideration
- Information should be interpreted in context of individual patient values

ProVent Model

300 patients ventilated 21 days at UNC

<table>
<thead>
<tr>
<th>Day 21 Variables</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressors</td>
<td>8.8 (1.6, 48.4)</td>
</tr>
<tr>
<td>Platelets ≤150</td>
<td>14.5 (4.1, 50.8)</td>
</tr>
<tr>
<td>Age ≥50</td>
<td>5.6 (2.4, 12.9)</td>
</tr>
<tr>
<td>Dialysis</td>
<td>2.9 (1.1, 7.7)</td>
</tr>
</tbody>
</table>

Carson et al. CCM 2008; 36:2061
## One-year Mortality

<table>
<thead>
<tr>
<th></th>
<th>Development</th>
<th>Validation</th>
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</thead>
<tbody>
<tr>
<td>Area under ROC</td>
<td>82</td>
<td>82</td>
</tr>
<tr>
<td>Sensitivity*</td>
<td>42</td>
<td>44</td>
</tr>
<tr>
<td>Specificity*</td>
<td>99</td>
<td>95</td>
</tr>
</tbody>
</table>

*Cutoff 90% likelihood of death
Validation Set

![Graph showing the reliability of predicted values with observed proportions, 95% CI, and perfect fit.]