The Norington Lecture

Dr Bradney W Norington, CBE
First President, Australian College of Rehabilitation Medicine
Australian Father of the Year, 1981

The important things to realise in rehabilitation are remaining abilities, not disabilities

PREP2: Tailoring upper limb rehabilitation after stroke

Cathy Stinear, PhD
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Department of Medicine
University of Auckland
Predictors of stroke outcome

- Stroke severity
- Age
- Co-morbidities
- Stroke lesion volume
- Leukoaraiosis

### Modified Rankin Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>Minor symptoms</td>
</tr>
<tr>
<td>2</td>
<td>Some restriction in lifestyle</td>
</tr>
<tr>
<td>3</td>
<td>Significant restriction in lifestyle</td>
</tr>
<tr>
<td>4</td>
<td>Partly dependent</td>
</tr>
<tr>
<td>5</td>
<td>Fully dependent</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
</tr>
</tbody>
</table>

Predictors of motor outcome

- Commonly impaired
- Critical for regaining independence
- Upper limb, age and stroke severity

Veerbeek et al. 2012

Motor function
Prediction is difficult

- Clinicians aren’t good at predicting outcomes based on clinical assessment alone
- Patients with similar acute performance can have very different outcomes

<table>
<thead>
<tr>
<th>ARAT SCORE</th>
<th>6 month prediction</th>
<th>Correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10</td>
<td>86%</td>
<td></td>
</tr>
<tr>
<td>10 - 56</td>
<td>47%</td>
<td></td>
</tr>
<tr>
<td>57</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>59%</td>
<td></td>
</tr>
</tbody>
</table>

Nijland et al., Physical Therapy, 2013

Mrs Smith

- 62 yo
- Right MCA ischaemic stroke 4 days ago
- MRC grades 0 to 1 throughout her left upper limb
- Works on a computer

Will my hand get better?
Biomarkers of the corticospinal tract can be useful

- Functional integrity
  - Transcranial magnetic stimulation
- Structural integrity
  - MRI

Functional outcomes

Kim & Weinstein, NNR, 2017
Biomarkers in clinical practice

- Efficient
- Accessible
- Categories not regression

Probability of arm recovery at 6 months = \( \frac{1}{1 + e^{-1.119 + 2.807 \text{FM - FE} + 2.149 \text{MI - SA}}} \)

Probability of moving a cup across the table at 6 months = \( \frac{1}{1 + e^{-4.8167 - 0.0533 \text{age} - 0.1240 \text{NIHSS}}} \)

Kwah & Herbert, Brain Sci, 2016

- Accounting for variance ≠ making individual predictions

Development of PREP2

- Biomarkers identified in 21 chronic patients
- Brain
- PREP developed in 40 subacute patients
- Brain
- PREP validated in 192 subacute patients
- Stroke
- PREP revised for clinical use in 207 subacute patients
- Ann Clin Transl Neural
- PREP2 implemented at ADHB
- Biomarkers of motor recovery reviewed
- Lancet Neurology
- Implementation of PREP2
- NeuroRehabilitation

PREP2 algorithm

- Hypothesis-free cluster analysis to identify categories of upper limb functional outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>57</td>
<td>50</td>
<td>57</td>
<td>113</td>
</tr>
<tr>
<td>Good</td>
<td>42</td>
<td>34</td>
<td>48</td>
<td>55</td>
</tr>
<tr>
<td>Limited</td>
<td>22</td>
<td>13</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>Poor</td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>23</td>
</tr>
</tbody>
</table>

- Hypothesis-free CART analysis to create a decision tree for predicting outcome, including factors:
  - age
  - sex
  - hand affected
  - thrombolysis
  - previous stroke
  - NIHSS score
  - UL therapy dose
  - stroke type
  - stroke location
  - SAFE score
  - MEP status (MEP+, MEP-)
  - CST damage with 5 MRI biomarkers
SAFE ≥ 5
3 days

SAFE score out of 10

< 80 y

EXCELLENT

SAFE ≥ 5
3 days
SAFE ≥ 8
3 days

SAFE < 8
3 days

< 80 y

SAFE ≥ 5
3 days

SAFE ≥ 5
3 days

EXCELLENT

GOOD
SAFE ≥ 5
3 days

SAFE ≥ 8
3 days

SAFE < 8
3 days

< 80 y

SAFE ≥ 5
3 days

SAFE ≥ 8
3 days

SAFE < 8
3 days

MEP+

4 – 7 days

EXCELLENT

GOOD

EXCELLENT

GOOD
Accurate for 75% of patients
<table>
<thead>
<tr>
<th>Prediction</th>
<th>Goal</th>
<th>Rehabilitation</th>
<th>Functional goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>Promote normal use</td>
<td>• Strength • Coordination • Fine control</td>
<td>• Avoid compensating with other hand • Shower as you normally would • Use both hands normally to make breakfast</td>
</tr>
<tr>
<td>Good</td>
<td>Promote function</td>
<td>• Strength • Coordination • Fine control</td>
<td>• Avoid compensating with other hand • Putting on shoes and socks</td>
</tr>
<tr>
<td>Limited</td>
<td>Promote movement</td>
<td>• Maintaining strength • Flexibility • Task adaptation • Bilateral practice</td>
<td>• Use both hands to wash face • Showering skills • Lifting a cup with both hands</td>
</tr>
<tr>
<td>Poor</td>
<td>Promote compensation</td>
<td>• Maintaining flexibility • Preventing shoulder instability or pain • Compensation</td>
<td>• Learn to write with other hand • Using one arm for upper body dressing • Using one hand to tie shoes</td>
</tr>
</tbody>
</table>
Who is PREP2 for?

- New upper limb weakness after stroke
  ✓ Previous stroke
  ✓ Haemorrhagic stroke
  ✓ Thrombolysis and thrombectomy

Stinear et al. 2017

Why use the PREP2 algorithm?

- Improves clinician confidence
- Enables tailoring of rehabilitation
- Improves rehabilitation efficiency
- Reduction in length of stay
  - 6 days (1 to 12 days)

Stinear et al. 2017
Why does length of stay drop?

- Therapists more confident to let mildly affected patients go
- Therapists tailor therapy more appropriately
  - Good prognosis – less passive movement
  - Poor prognosis – less task specific training
- Therapists more confident to move to compensation for patients with a poor prognosis

What happens after 3 months?

- PREP2 predictions accurate at 2y for 80% of participants
  - About 10% do better than expected
  - About 10% do worse than expected

- PREP2 category stayed stable between 3m and 2y for 83% of participants

- PREP2 category changed for 17% of participants
  - all with a Good or Excellent prediction

- PREP2 predictions are accurate at both 3m and 2y after stroke
What are the risks?

- Safety
  - TMS approved by physician
- Negative predictions
  - Preparation and skill, patient support
- Being wrong
  - Careful language, not wrong by much

What are the costs?

- Implementation
  - Leadership, stakeholder engagement, initial training, resources
- Clinical use
  - Therapist time
- Ongoing training
  - New staff and refreshers for existing staff
How we can help

- Training
- Resources
- www.presto.auckland.ac.nz

Mrs Smith

- 62 yo
- 4 days post stroke
- MRC grades 0 to 1 throughout her left upper limb
- Works on a computer
- MEP+ therefore a GOOD prognosis
- At 12 weeks: ARAT score of 47
  Returned to work part-time
Conclusions

Biomarkers for patient selection in trials

Biomarkers in clinical practice

Personalised rehabilitation

Better outcomes

Thanks

Patients and their families
Dr Marie-Claire Smith
Dr Suzanne Ackerley
Professor Winston Byblow
Professor Alan Barber
Allied health, nursing and medical teams at ADHB

www.presto.auckland.ac.nz

PRESOT
Predict Stroke Outcomes