Predicting stroke recovery

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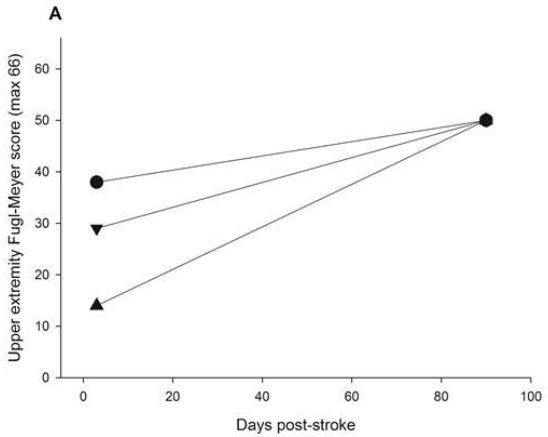
Predictors of stroke outcome

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

Predictors of motor recovery and outcome

Modified Rankin Scale	
Grade	Description
0	No symptoms
1	Minor symptoms
2	Some restriction in lifestyle
3	Significant restriction in lifestyle
4	Partly dependent
5	Fully dependent
6	Dead

Recovery and Outcome



Different recovery
Same outcome

Impairment and Function

Impairment

- Voluntary movement
- Fugl-Meyer scale (FM)

Function

- Task completion
- Action Research Arm Test (ARAT)
- Functional Ambulation Category (FAC)

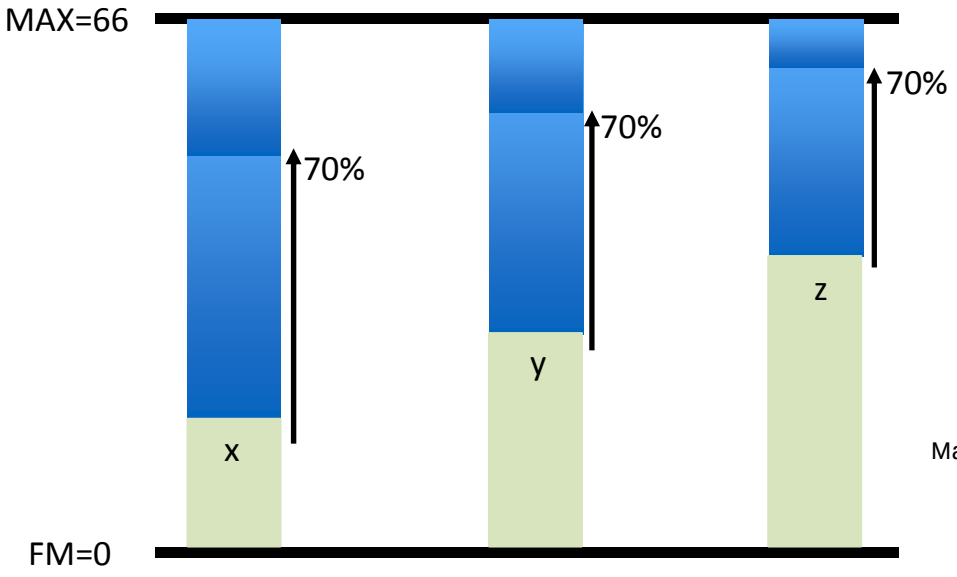
Today

Predicting recovery from impairment

Predicting functional outcomes

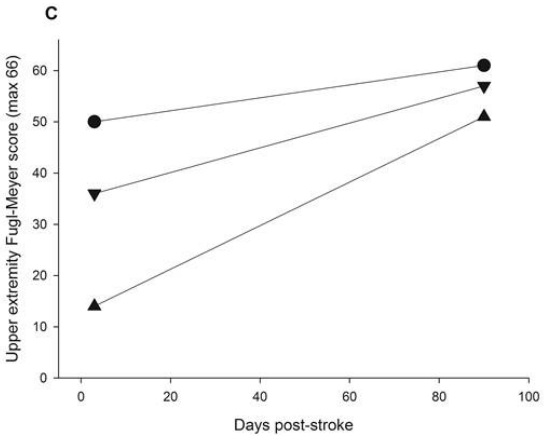
Recovery from impairment

Fugl-Meyer scores increase by 70% of the available improvement for most patients



Prabhakaran et al., NNR, 2008
Marshall et al., Ann Neurol, 2009
Winters et al., NNR, 2014
Feng et al., Ann Neurol, 2015
Buch et al., Neurology, 2016

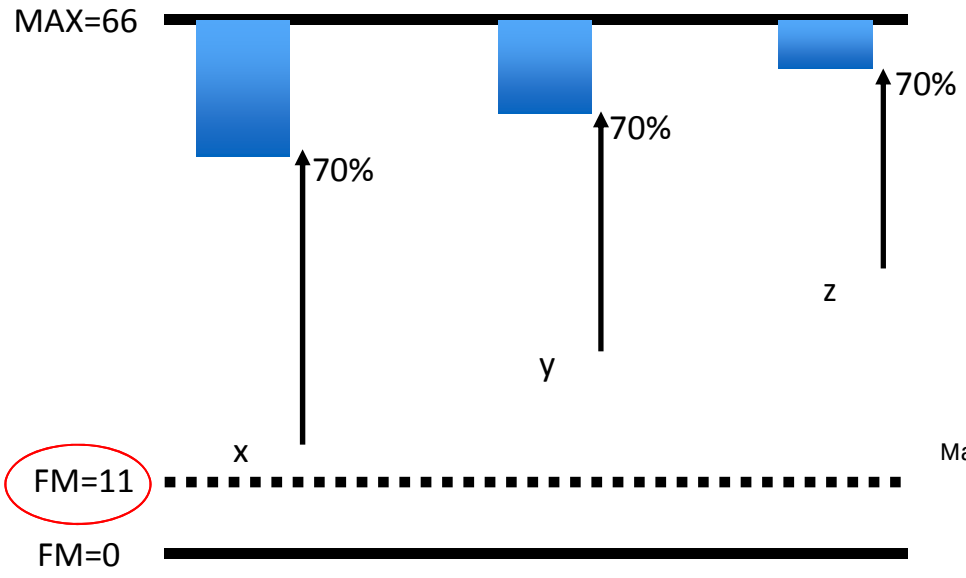
Recovery and Outcome



Same ***proportional*** recovery
Different outcome

Recovery from impairment

Fugl-Meyer scores increase by 70% of the available improvement for most patients



Prabhakaran et al., NNR, 2008
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Recovery from impairment

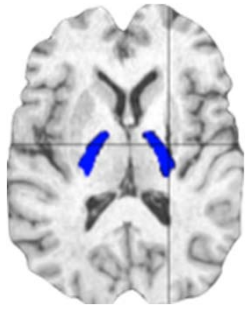
Biomarkers of the corticospinal tract can be useful

Functional integrity

- Transcranial magnetic stimulation

Structural integrity

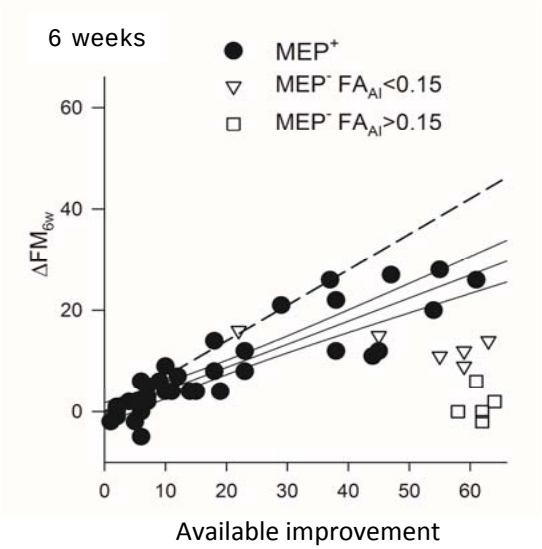
- Magnetic resonance imaging



Recovery from impairment

FM scores increase by 70% of the available improvement for patients with a **functional corticospinal tract**

Byblow et al., Ann Neurol, 2015

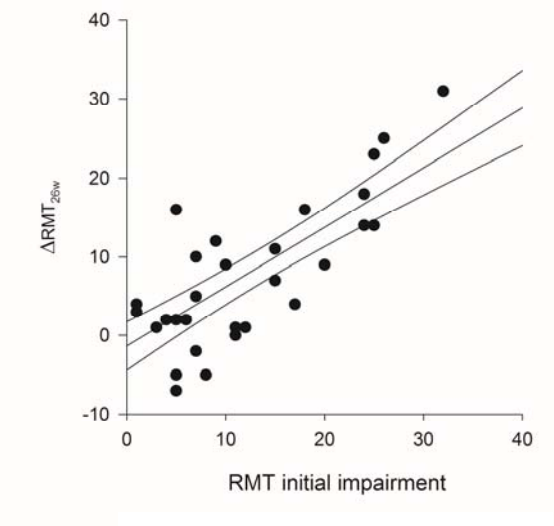


β = 0.45, 95% CI = 0.39 – 0.50

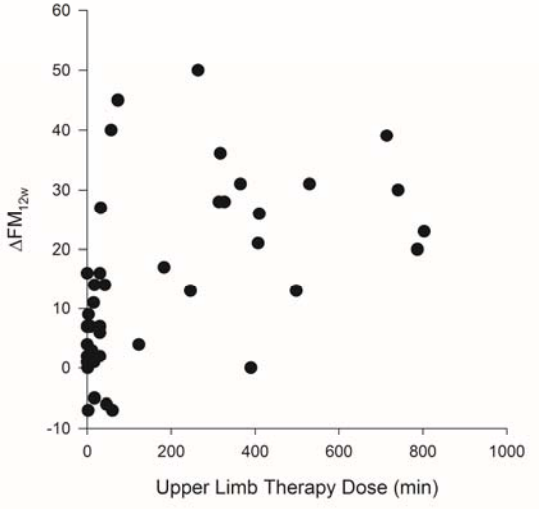
Recovery from impairment

Excitability of the stroke M1 also increases by 70% of the available improvement

Recovery from impairment is not related to therapy dose



β = 0.74, 95% CI = 0.64 – 0.85

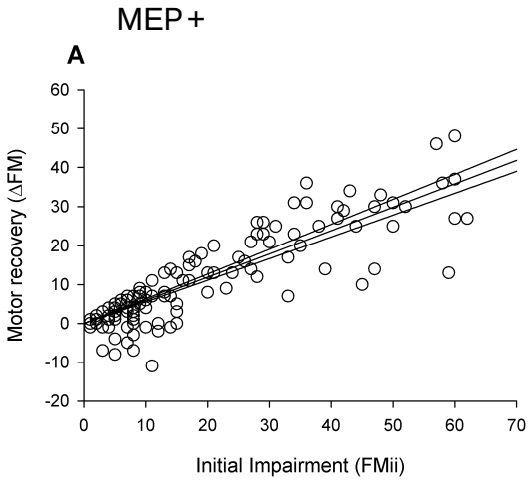


Byblow et al., Ann Neurol, 2015

Recovery from impairment

FM scores increase by 70% of the available improvement
for patients with a **functional corticospinal tract**

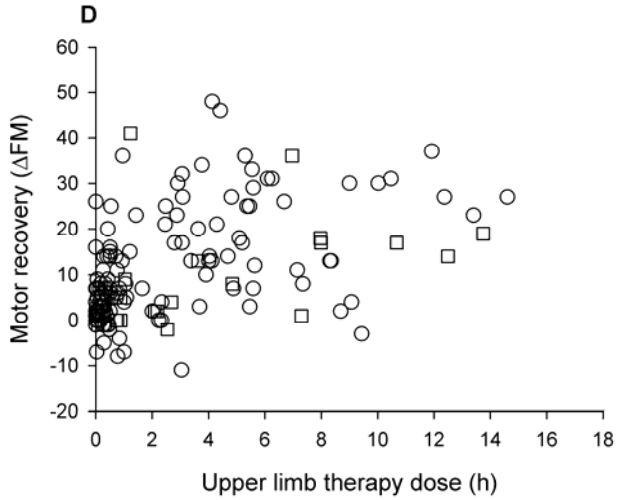
Stinear et al., Stroke, 2017



β = 0.63, 95% CI = 0.55 – 0.70

Recovery from impairment

Recovery from impairment is not related to therapy dose

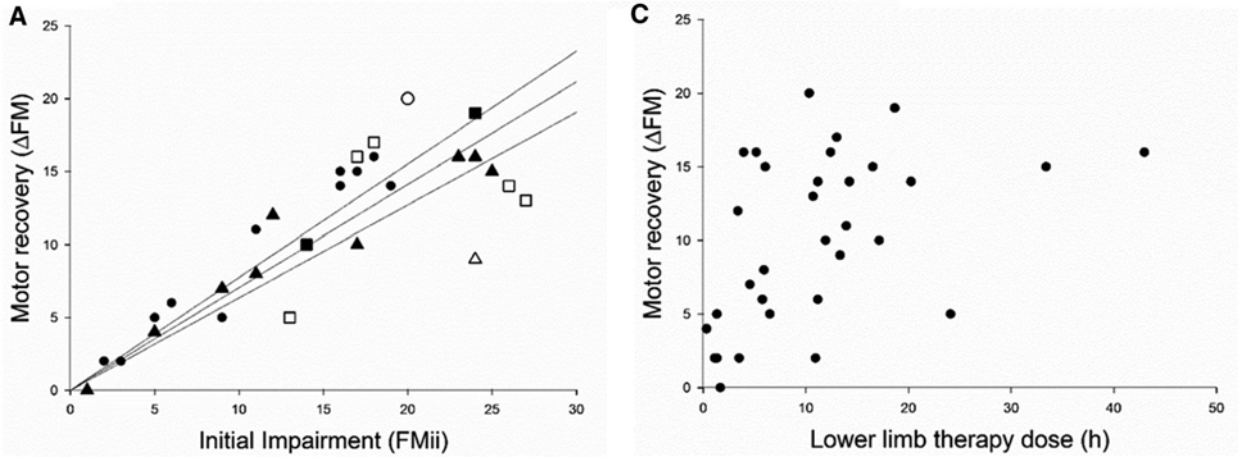


Stinear et al., Stroke, 2017

Recovery from LL impairment

Lower limb Fugl-Meyer scores increase by 70% of the available improvement for all patients, regardless of MEP status

Recovery from lower limb impairment is not affected by therapy dose



Smith et al., Stroke, 2017

Recovery from impairment

Recovery from impairment reflects a spontaneous neurobiological recovery process with which current doses of therapy do not interact

Inter-individual Variability in the Capacity for Motor Recovery After Ischemic Stroke
Shyam Prabhakaran, Eric Zarahn, Claire Riley, Allison Speizer, Ji Y. Chong, Ronald M. Lazar, Randolph S. Marshall and John W. Krakauer
Neurorehabil Neural Repair 2008 22: 64 originally published online 8 August 2007
DOI: 10.1177/1545968307305302

Clinical Research Article

Generalizability of the Proportional Recovery Model for the Upper Extremity After an Ischemic Stroke

Neurorehabilitation and Neural Repair
2015, Vol. 29(7) 614-622

DOI: 10.1177/1545968314562115
nnr.sagepub.com
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Caroline Winters, MSc[1], Erwin E. H. van Wegen, PhD[1], Andreas Daffertshofer, PhD[2], and Gert Kwakkel, PhD[1,3]

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Sviatlana Rizk, PhD
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Leonardo G. Cohen, MD
Armin Schnider, MD
Adrian G. Guggisberg, MD

PREDICTING MOTOR IMPROVEMENT AFTER STROKE WITH CLINICAL ASSESSMENT AND DIFFUSION TENSOR IMAGING

Reliable predictors of motor improvement in individual patients after stroke are scarce. Acute determination of upper limb Fugl-Meyer assessment (FMA) appears to have predictive value.[1,2] This approach predicts that pa-

Corticospinal Tract Lesion Load: An Imaging Biomarker for Stroke Motor Outcomes

Wuwei Feng, MD, MS,[1,5] Jasmine Wang, BA,[2] Pratik Y. Chhatbar, MD, PhD,[1] Christopher Doughty, MD,[2] Douglas Landsittel, PhD,[3] Vasileios-Arsenios Lioutas, MD,[2] Steven A. Kautz, PhD,[4,5] and Gottfried Schlaug, MD, PhD[2]

Proportional Recovery After Stroke Depends on Corticomotor Integrity

Winston D. Byblow, PhD,[1,2] Cathy M. Stinear, PhD,[1,3] P. Alan Barber, MBChB, PhD,[1,3] Matthew A. Petoe, PhD,[1,3,4] and Suzanne J. Ackerley, BPhty, PhD[1,3]

Proportional Recovery From Lower Limb Motor Impairment After Stroke

Stroke

Marie-Claire Smith, BHSc; Winston D. Byblow, PhD; P. Alan Barber, PhD; Cathy M. Stinear, PhD

Proportional Motor Recovery After Stroke
Implications for Trial Design

Stroke

Cathy M. Stinear, PhD; Winston D. Byblow, PhD; Suzanne J. Ackerley, PhD; Marie-Claire Smith, BHSc; Victor M. Borges, PhD; P. Alan Barber, PhD, FRACP

What does this mean?

Clinical research

Aim to increase the proportion above 70%

If patients have less residual impairment, they will have greater function, independence, and quality of life

Use TMS to select patients for UL trials

Clinical practice ?

Most patients are left with residual impairment

Patients with severe UL impairment can recover proportionally if MEP+

Current therapy helps patients learn to function as well as possible

The big picture

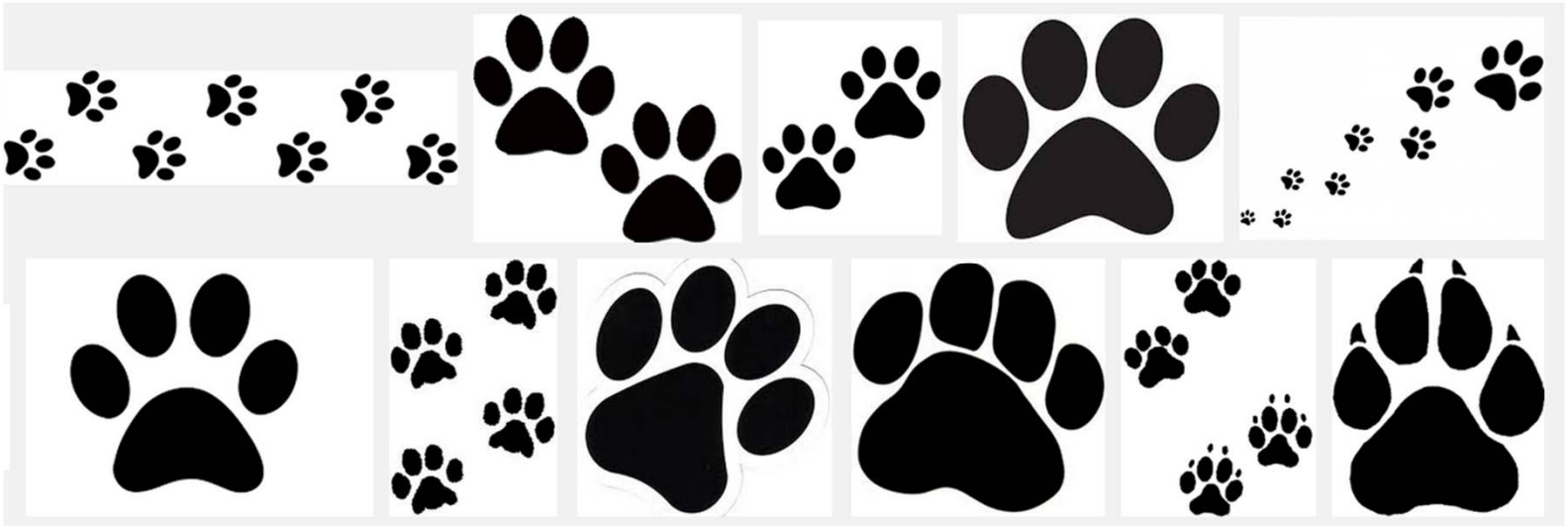
Eight multi-centre RCTs of motor rehabilitation since 2011

- Acute and sub-acute stage
- Total 1,795 patients
- Variations of current practice
- All neutral

How can we increase sensitivity to intervention effects at the sub-acute stage?

- Greater contrast
- Patient selection

Prediction of motor recovery after stroke: advances in biomarkers
Cathy M Stinear
Lancet Neurol 2017; 16: 826–36
THE LANCET Neurology



How does better prediction of functional outcomes help?

MANAGE PATIENT EXPECTATIONS

TAILOR REHABILITATION GOALS

USE TIME AND RESOURCES TO BRING THE BEST OUTCOME FOR THE PATIENT

How good are we at predicting now?

> 31,000 patients discharged from > 900 US hospitals

There is a 3-fold variation in discharge rates to SNF and IRF after stroke, even after adjusting for clinical characteristics and geographic availability

Zian et al. Stroke 2017;48:2836-42

“This marked variation could reflect the lack of an evidence-based algorithm…”

How good are we at predicting now?

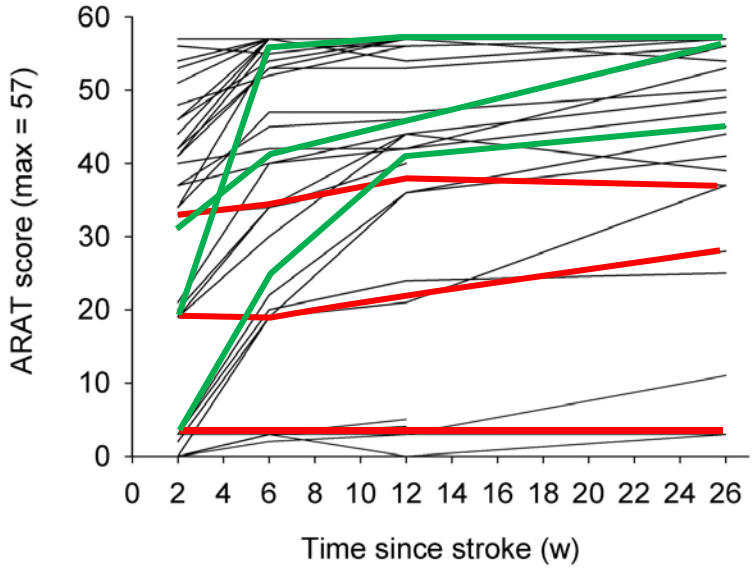
Predicting ARAT score at 6 months
(Action Research Arm Test)

6 month prediction	Correct
<10	86%
10 - 56	47%
57	61%
Overall	**59%**

Nijland et al., Physical Therapy, 2013

Functional recovery and outcomes

Patients who have initially similar clinical scores can have very different recoveries and outcomes




BRAIN

The PREP algorithm predicts potential for upper limb recovery after stroke

Stinear et al., Brain, 2012

Functional outcomes

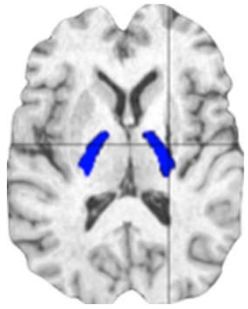
Biomarkers of the corticospinal tract can be useful

Functional integrity

- Transcranial magnetic stimulation

Structural integrity

- Magnetic resonance imaging



PREP2 algorithm

PREP- Previously developed and validated

Revised with data from 207 patients

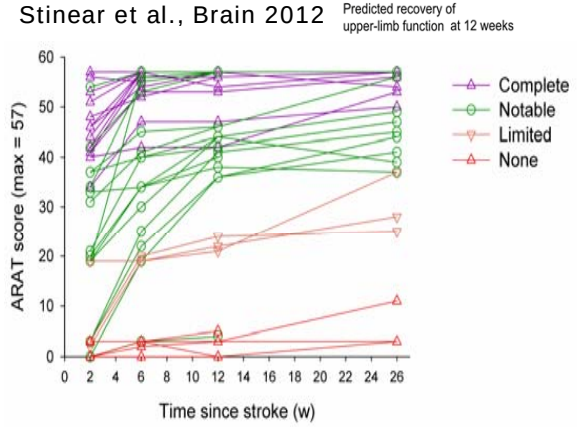
Median age 72 y (18 – 98 y)

- 50% female
- 10% ICH
- 13% previous stroke

Recruited within 72 h of stroke symptom onset
Usual care, therapy dose recorded

Primary endpoint: ARAT score 3 m post-stroke

Stinear et al., Brain 2012



PREP2 algorithm

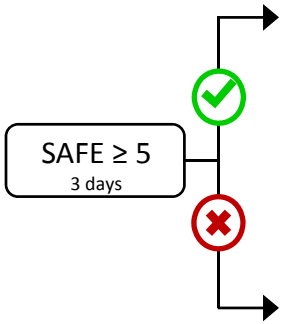
Hypothesis-free cluster analysis of ARAT scores at 3 m to identify four levels of upper limb function

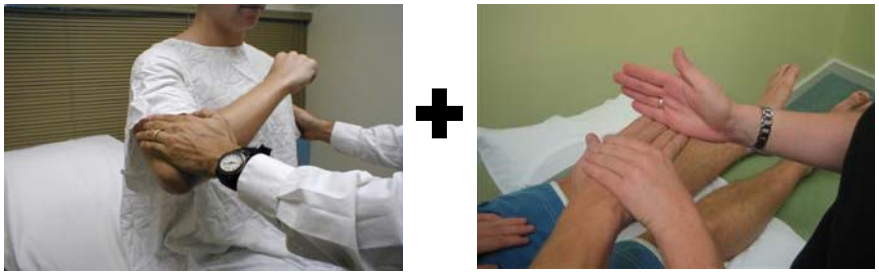
Outcome	Mean	Median	Minimum	Maximum	N
Excellent	56	57	50	57	113
Good	43	42	34	48	55
Limited	22	22	13	31	16
Poor	2	0	0	7	23

Classification and regression tree (CART) analysis to create a decision tree for predicting outcome, including factors:

age	gender	hand affected	SAFE score
thrombolysis	previous stroke	NIHSS score	MEP status (MEP+, MEP-)
UL therapy dose	PLIC FAAI	CST lesion load (%)	SMT lesion load (%)
stroke type (LACI, PACI, TACI, POCI, ICH)		stroke location (subcortical, cortical/subcortical)	

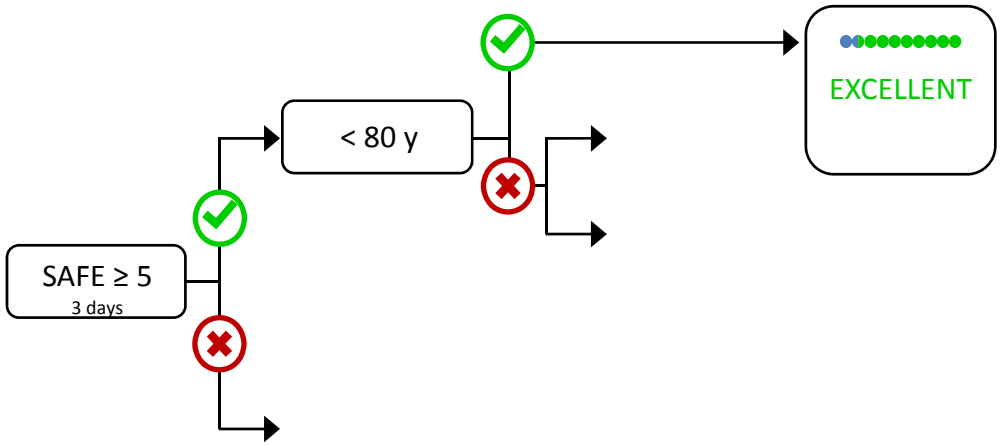
PREP2 algorithm



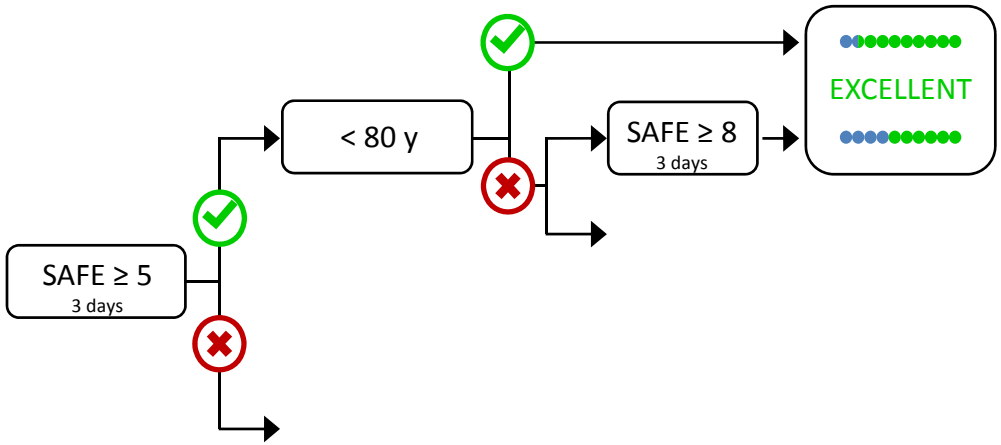


SAFE score out of 10

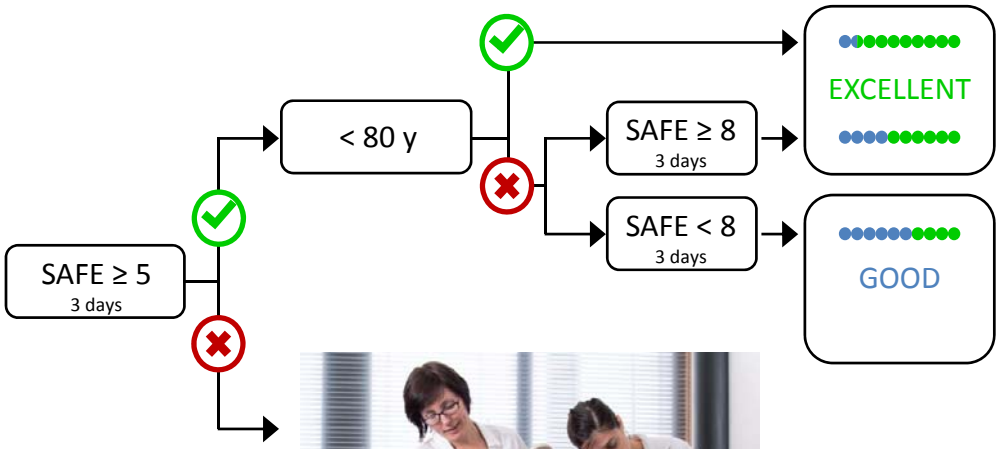
PREP2 algorithm



PREP2 algorithm



PREP2 algorithm



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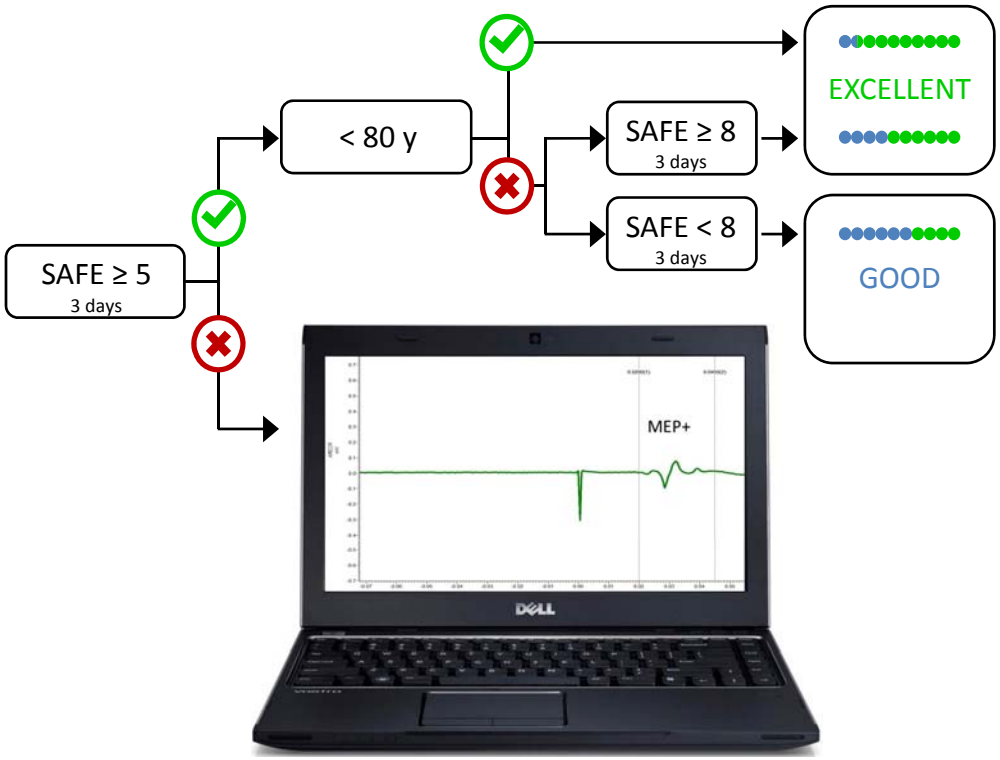
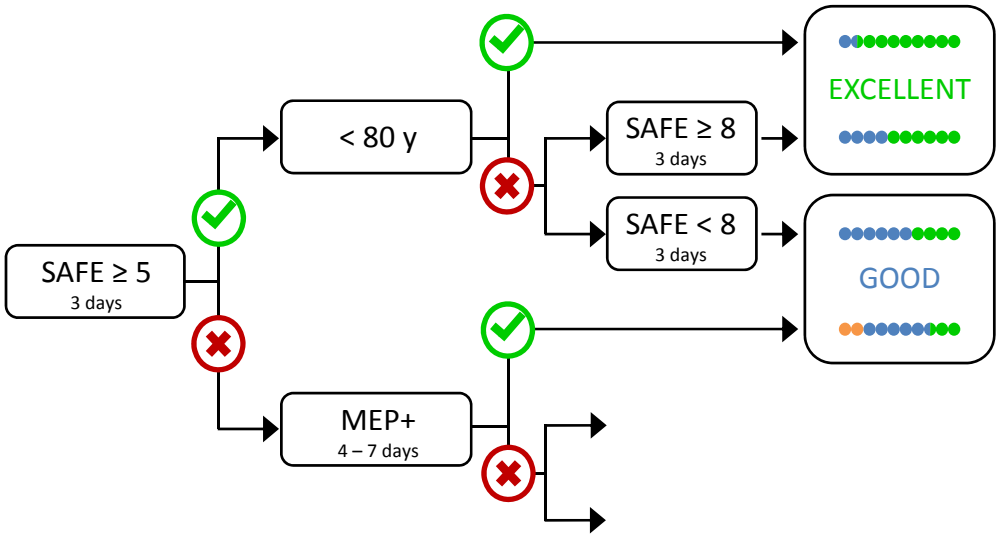


PREP2 algorithm



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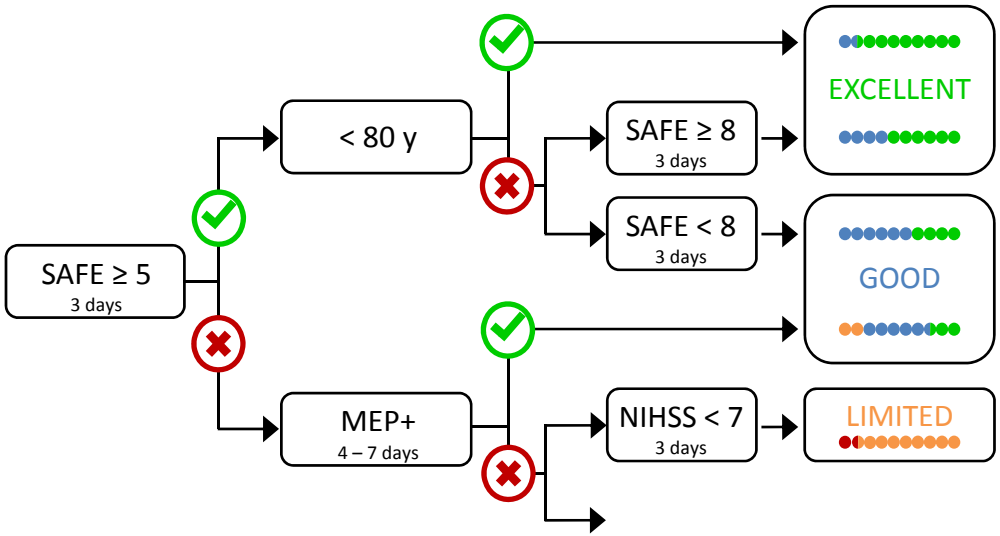

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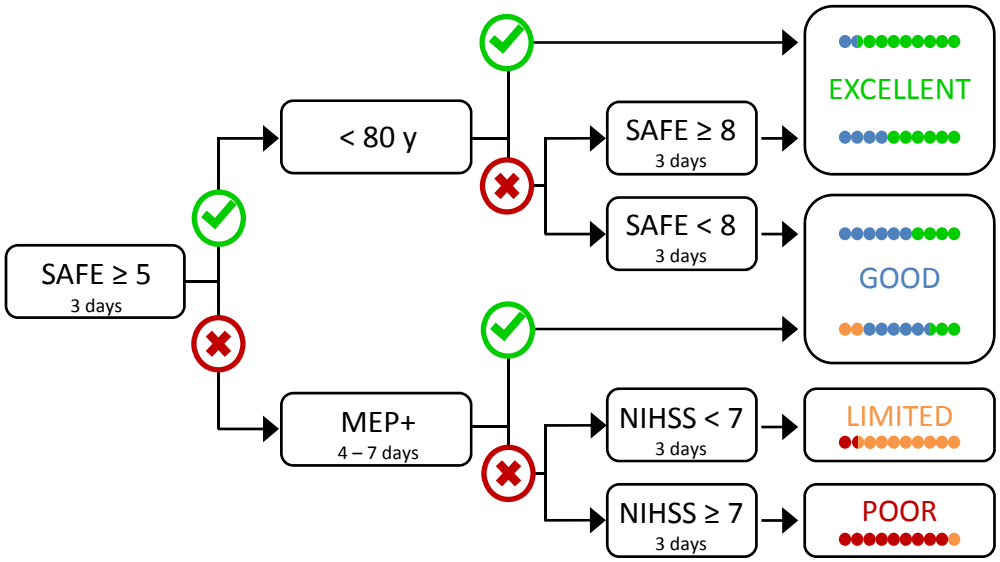


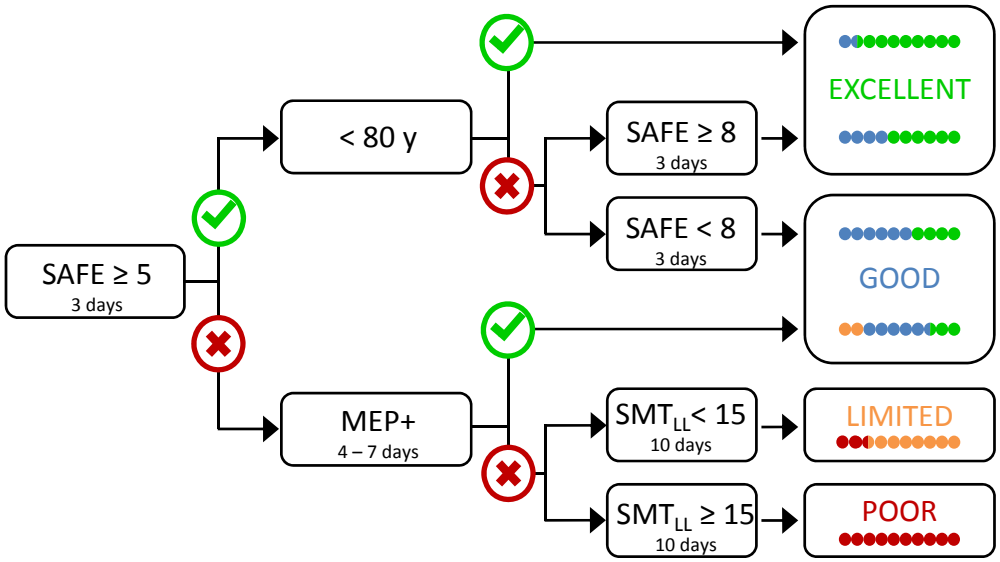
Accurate for
75% of patients

ANNALS of Clinical and Translational Neurology

PREP2: A biomarker-based algorithm for predicting upper limb function after stroke

Cathy M. Stinear[1,2], Winston D. Byblow[2,3], Suzanne J. Ackerley[1,2], Marie-Claire Smith[1,2], Victor M. Borges[1,2] & P. Alan Barber[1,2,4]

PREP2 algorithm



Also accurate for 75% of patients

ANNALS of Clinical and Translational Neurology

PREP2: A biomarker-based algorithm for predicting upper limb function after stroke

Cathy M. Stinear[1,2], Winston D. Byblow[2,3], Suzanne J. Ackerley[1,2], Marie-Claire Smith[1,2], Victor M. Borges[1,2] & P. Alan Barber[1,2,4]

PREP2 algorithm

Excellent - Promote normal use

Good - Promote function

Limited - Promote movement

Poor - Promote compensation

What happens when you use it?

PREP information changed therapist perceptions and behavior

Therapist confidence

Higher with PREP information p = 0.046

What happens when you use it?

PREP information altered therapy content

Less passive movement for patients with Excellent prognosis

Less task specific training for patients with Limited or Poor prognosis

PREP infor

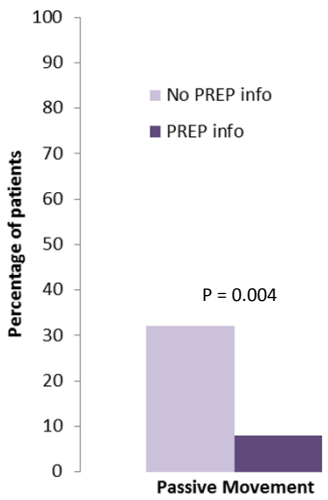
Lower th

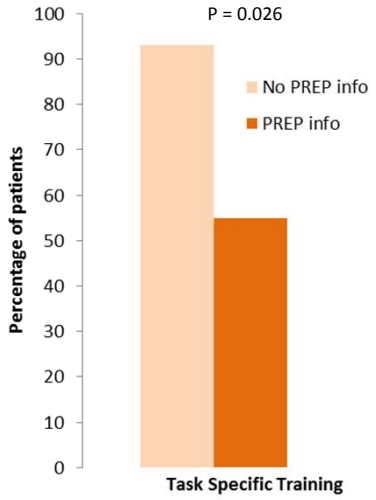
No effec

As intended

PREP alt

PREP dic





What happens when you use it?

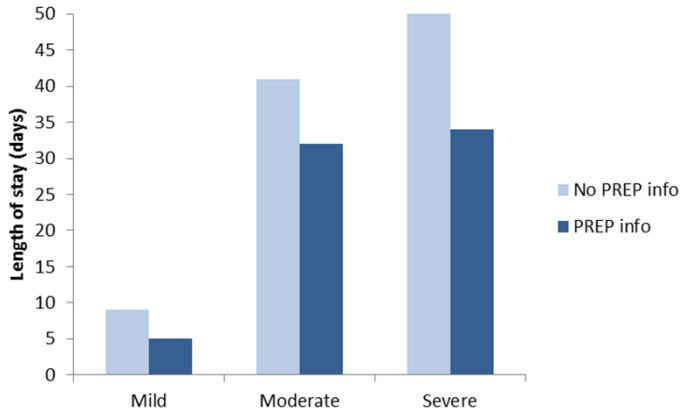
PREP information shortened length of stay

Stroke severity: Longer stays for more severe stroke, $p < 0.001$

PREP: Shorter stays with PREP information, $p = 0.005$

*Median decrease of **6 days**, 95% CI = 1 – 12 days*

No background change, p = 0.843



What happens when you use it?

No effects of PREP information on clinical outcomes

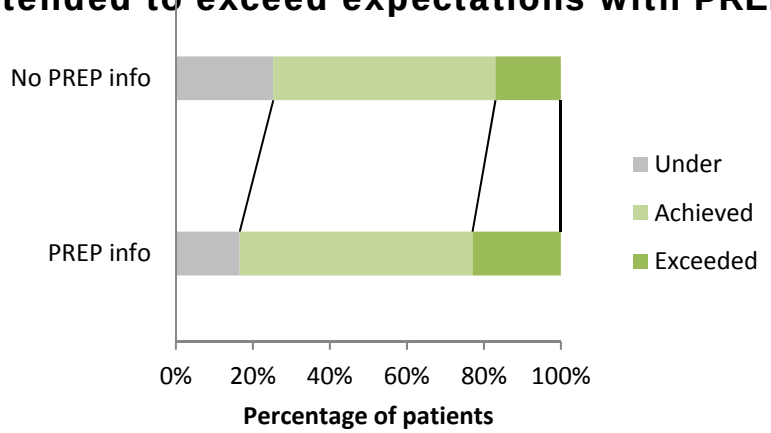
Similar ARAT scores at 12 weeks, p = 0.51

Similar mRS scores at 12 weeks, p = 0.85

Similar MAL scores at 6 months, p = 0.25

Similar SIS scores at 6 months, p = 0.38

Patients tended to exceed expectations with PREP information



What happens when you use it?

PREP algorithm information gave therapists more **confidence**

More **focused** upper limb rehabilitation, **tailored** to the recovery potential of **individual** participants, may have contributed to **shortened length of stay** by around 1 week

PREP information may **increase rehabilitation efficiency**, with no negative effects on patient outcomes

Predicting Recovery Potential for Individual Stroke Patients Increases Rehabilitation Efficiency

Stroke

Cathy M. Stinear, PhD; Winston D. Byblow, PhD; Suzanne J. Ackerley, PhD; P. Alan Barber, PhD; Marie-Claire Smith, BHSc


MUST
GO
FASTER

Walking function after stroke

60% of patients need help to walk

Independent walking is the most frequent goal

Determines WHEN a patient will be discharged from rehabilitation and WHERE they will go

Marie-Claire Smith
A freshly-minted PhD!

Predictors

Balance
Strength
Age
Comorbidities

Neurorehabilitation and Neural Repair

ASNR AMERICAN SOCIETY OF NEUROREHABILITATION

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Original Article

The TWIST Algorithm Predicts Time to Walking Independently After Stroke

Marie-Claire Smith, BHSc, **P. Alan Barber**, Phd, **Cathy M. Stinear**, PhD

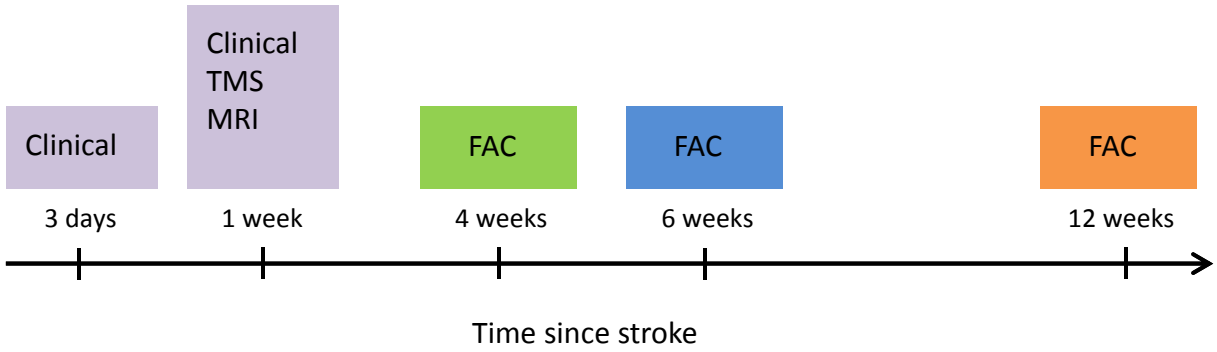
https://doi-org.ezproxy.auckland.ac.nz/10.1177/1545968317736820 | First Published November 1, 2017

FAC	Functional Ambulation Categories
0	Not walking or 2 assist
1	Mod-max 1 assist
2	Minimal 1 assist
3	Supervision only
4	Independent on level surfaces
5	Independent on stairs, slopes, uneven surfaces

Demographics and stroke characteristics (n = 41)	
Age (median, range)	72 (43-96)
Female	24 (59%)
First stroke	37 (90%)
Haemorrhage	6 (15%)
tPA	6 (15%)
Stroke severity	
Mild (NIHSS <5)	7 (17%)
Moderate – severe (NIHSS ≥ 5)	34 (83%)

Clinical	
Ambulation	
Non-ambulatory (FAC = 0)	33 (80%)
Dependent ambulation FAC (1,2,3)	8 (20%)
Motricity index LL (median out of 100, range)	48 (0-92)

Study timeline



Variables entered into analysis: age, sex, stroke classification (Oxfordshire), NIHSS, stroke type (motor, motor-sensory, motor-sensory-hemianopia), comorbidities, FAC, MRC grades, Motricity Index, Trunk Control Test, therapy dose, therapy intensity (minutes per day), MEP status, MRI lesion load.

TWIST algorithm

Trunk Control Test

0 points = requiring assistance

12 points = indep but abnormal movement pattern

25 points = indep and normal movement pattern

1) Roll to weak side
2) Roll to strong side
3) Lie to sit
4) Sitting, feet off floor 30 seconds

TWIST algorithm

Accurate for 95% of patients

Predicting Recovery of function

Baseline clinical scores alone are poor predictors of UL functional outcome

The PREP2 algorithm can accurately predict upper limb functional outcome for 75% of patients

TMS is essential for patients with a SAFE score < 5

Clinical scores may be reasonable predictors of independent walking

The TWIST algorithm might accurately predict whether and when patients will recovery independent walking, but needs validation

TMS might not be needed

What does this mean?

Clinical practice

- For Upper limb:
- You can make an accurate UL prediction for 2/3 of patients with SAFE score and Age
- If on day 3 SAFE < 5, get NIHSS score and book TMS
- Tailor therapy according to predicted outcome

- For Lower limb:
- You might be able to make an accurate prediction for most patients with TCT and hip extension
- Manage discharge planning and patient expectations

What does this mean?

Clinical research

Match treatment and control groups based on predicted outcome, not just baseline characteristics

Conclusions

Biomarkers for patient selection in trials

Biomarkers in clinical practice

Personalised rehabilitation

Better outcomes

Thanks

www.presto.auckland.ac.nz

Associate Professor Cathy Stinear
Dr Suzanne Ackerley
Marie-Claire Smith
Dr Victor Borges
Professor Alan Barber

Anna McRae
Ben Scrivener
Kathryn Quick
Emma Monigatti
Claire Valentine
Desiree McCracken

Winston Byblow @MyPlasticBrain
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