Predicting Recovery Potential for Individual Stroke Patients Increases Rehabilitation Efficiency

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Background and Purpose—Several clinical measures and biomarkers are associated with motor recovery after stroke, but none are used to guide rehabilitation for individual patients. The objective of this study was to evaluate the implementation of upper limb predictions in stroke rehabilitation, by combining clinical measures and biomarkers using the Predict Recovery Potential (PREP) algorithm.

Methods—Predictions were provided for patients in the implementation group (n=110) and withheld from the comparison group (n=82). Predictions guided rehabilitation therapy focus for patients in the implementation group. The effects of predictive information on clinical practice (length of stay, therapist confidence, therapy content, and dose) were evaluated. Clinical outcomes (upper limb function, impairment and use, independence, and quality of life) were measured 3 and 6 months poststroke. The primary clinical practice outcome was inpatient length of stay. The primary clinical outcome was Action Research Arm Test score 3 months poststroke.

Results—Length of stay was 1 week shorter for the implementation group (11 days; 95% confidence interval, 9–13 days) than the comparison group (17 days; 95% confidence interval, 14–21 days; P=0.001), controlling for upper limb impairment, age, sex, and comorbidities. Therapists were more confident (P=0.004) and modified therapy content according to predictions for the implementation group (P<0.05). The algorithm correctly predicted the primary clinical outcome for 80% of patients in both groups. There were no adverse effects of algorithm implementation on patient outcomes at 3 or 6 months poststroke.

Conclusions—PREP algorithm predictions modify therapy content and increase rehabilitation efficiency after stroke without compromising clinical outcome.

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Key Words: length of stay ■ prognosis ■ stroke ■ upper extremity

Recovery of motor function after stroke is difficult to predict for individuals.[1] Patients with similar initial motor impairment may achieve widely disparate levels of motor function and independence.[2] Clinical measures of initial motor impairment,[3] neurophysiological biomarkers of corticospinal tract function, and neuroimaging biomarkers of direct and indirect descending motor pathways (herein referred to as corticomotor) are related to motor outcomes.[4] Transcranial magnetic stimulation (TMS) has been used to test the function of the ipsilesional lateral corticospinal tract projecting to distal muscles of the paretic upper and lower limbs. At the subacute stage, patients in whom TMS can elicit motor evoked potentials (MEPs) typically experience greater motor recovery and better outcomes than those in whom MEPs cannot be elicited.[5–8] Magnetic resonance imaging has been used to evaluate the effects of stroke on the structure of corticomotor pathways. At the subacute stage, patients whose ipsilesional corticomotor pathways have less overlap with the stroke lesion typically experience greater motor recovery and better outcomes.[9,10] Similarly, patients whose mean fractional anisotropy and diffusivity measures are more symmetrical between the ipsilesional and contralesional corticomotor pathways also experience better motor outcomes.[11,12] These studies show that clinical measures and biomarkers have consistent relationships with future motor function. However, none have been implemented in routine clinical practice to guide rehabilitation therapy for individual patients.

The Predict Recovery Potential (PREP) algorithm combines clinical measures and neurophysiological and neuroimaging biomarkers that are sensitive to corticomotor pathway

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integrity to predict likely upper limb functional outcome.[1,2] It does so in a sequential way, starting by summing the Medical Research Council grades for shoulder abduction and finger extension (SAFE) strength within 3 days of stroke symptom onset. For patients with a summed SAFE score <8 (out of 10), the functional integrity of the corticospinal tract is evaluated by determining the presence or absence of paretic upper limb MEPs using TMS. For patients without MEPs, the microstructural characteristics of corticomotor pathways are evaluated with diffusion tensor imaging (Figure 1). The algorithm predicts 1 of 4 possible upper limb functional outcomes for each patient: Excellent, Good, Limited, or None. These categories are based on the Action Research Arm Test (ARAT) score at 3 months poststroke.[2]

The aim of this study was to evaluate the implementation of upper limb predictions in stroke rehabilitation. Therapists and patients were provided with PREP algorithm predictions, and therapists were free to choose the content and dose of upper limb therapy. We expected the algorithm to provide accurate predictions of upper limb function, and that therapists would use this information to modify upper limb therapy and improve rehabilitation efficiency.

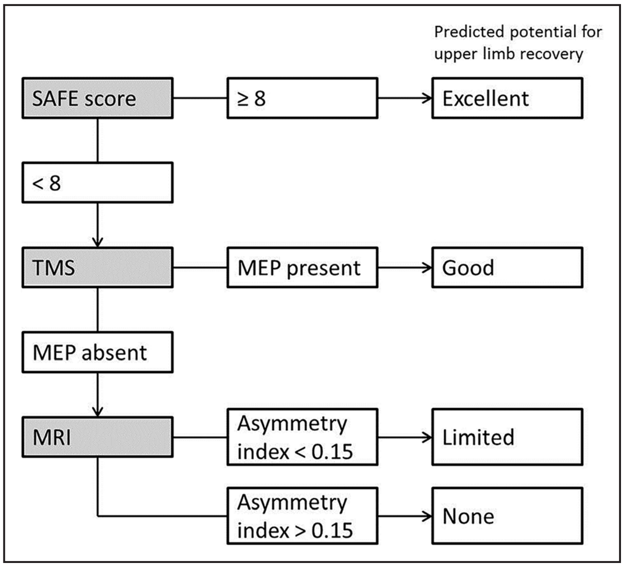

Figure 1. Predict Recovery Potential (PREP) algorithm. The algorithm begins with an assessment of paretic shoulder abduction and wrist extension strength, using Medical Research Council grades. If the sum of these grades (the Shoulder Abduction and Finger Extension [SAFE] score) is ≥8 within 72 hours after stroke, the patient is predicted to have potential for Excellent upper limb function within 3 months. If the SAFE score is <8, transcranial magnetic stimulation (TMS) is used to assess the functional integrity of the ipsilesional lateral corticospinal tract, ≈5 to 7 d poststroke. If TMS can elicit motor evoked potentials (MEPs) in the paretic wrist extensor or first dorsal interosseous muscles (MEP+), then the patient is predicted to have potential for Good upper limb function within 3 months. If TMS cannot elicit MEPs, a diffusion-weighted magnetic resonance imaging (MRI) scan is obtained ≈10 d poststroke. The mean fractional anisotropy is calculated in the posterior limbs of the internal capsules, and an asymmetry index calculated. If the asymmetry index is <0.15, the patient is predicted to have potential for Limited upper limb function within 3 months. If the asymmetry index is ≥0.15, the patient's potential for recovery of upper limb function is predicted to be None. Description of the 4 prediction categories and the suggested rehabilitation focus for each are given in Table 1.

Methods

Study Design

First ever or recurrent ischemic stroke and intracerebral hemorrhage patients with new upper limb weakness, as determined by the attending neurologist, and aged ≥18 years were recruited at a public tertiary care hospital. Patients with cerebellar stroke, contraindications to TMS and magnetic resonance imaging, or cognitive or communication impairment precluding informed consent, were excluded. The study was approved by the national ethics committee, and written informed consent obtained from all patients.

The PREP algorithm was used to predict likely upper limb functional outcome. The study had 2 phases. PREP algorithm predictions were withheld from clinicians and patients during recruitment of the comparison group. Predictions were provided to clinicians and patients during recruitment of the implementation group. Randomization into groups where predictions were withheld or provided was not performed in this single-site study, to avoid practice creep and study contamination. Implementation of the PREP algorithm in clinical practice began after the comparison group was recruited.

PREP Algorithm

A SAFE score out of 10 was determined for the paretic upper limb by summing the Medical Research Council grades for these movements (Figure 1),[1,2] which were separately scored out of 5 through full range of motion, without + or − qualifiers. The scores were summed for a SAFE score out of 10. Finger extension was graded based on the performance of the majority of digits if the strength varied across digits. The PREP algorithm predicted an Excellent upper limb outcome within 3 months if the patient achieved a SAFE score of ≥8 by day 3 poststroke. The day of symptom onset was counted as day zero, and the SAFE score obtained at least once before or on day 3. If the SAFE score was <8 before day 3, it was obtained again on day 3.

For patients with a SAFE score <8, TMS was used to test the functional integrity of the ipsilesional lateral corticospinal tract 7 days poststroke, as previously described.[2] In brief, MEPs were recorded from the paretic extensor carpi radialis and first dorsal interosseous muscles with surface electromyography. Researchers trained and supervised therapists to carry out this assessment for implementation group patients. If no MEP was obtained with 100% stimulator output and the patient at rest, they voluntarily gripped their nonparetic hand and attempted to do so with their paretic hand, to facilitate a response. The patient was categorized as MEP positive (MEP+) if MEPs of any amplitude were consistently observed in either muscle, either at rest or with preactivation. The algorithm predicted a Good upper limb outcome within 3 months for MEP+ patients.

For patients without MEPs (MEP−), diffusion-weighted magnetic resonance imaging was used to evaluate the microstructural characteristics of corticomotor pathways 12 days poststroke.[2] An asymmetry index was calculated from the mean fractional anisotropy of the posterior limb of each internal capsule, to provide a prediction of either Limited or None upper limb function within 3 months.[2]

The PREP prediction describes the minimum level of function expected within 3 months and was provided for the implementation group with a recommended focus for upper limb rehabilitation (Table 1). This information was provided to therapists in a standardized written form and discussed with the patient and their family. Care was taken to explain that the prediction was not a guaranteed outcome, and that some people might recover better or worse than expected. The prediction described the minimum level of movement or function they could expect to achieve within 3 months. It was also explained that the prediction's purpose was to provide a realistic rehabilitation focus at this early stage of recovery, which could be revised at a later stage by their therapists.

Clinical Practice Measures

The primary clinical practice outcome was inpatient length of stay, defined as the total number of nights spent in the acute and rehabilitation wards. Secondary outcomes were therapists' confidence

Table 1. Upper Limb Predictions and Rehabilitation Focus

Category	Upper Limb Prediction	Upper Limb Rehabilitation Focus
Excellent	Potential to make a complete, or near-complete, recovery of hand and arm function within 3 months.	Promote normal use of the affected hand and arm with task-specific practice, while minimizing compensation with the other hand and arm.
Good	Potential to be using their affected hand and arm for most activities of daily living within 3 months, though they may continue to experience some weakness, slowness, or clumsiness.	Promote normal function of the affected hand and arm by improving strength, coordination, and fine motor control with repetitive and task-specific practice. Emphasis is placed on minimizing compensation with the other hand and arm, and the trunk.
Limited	Potential to regain movement in their hand and arm within 3 months, but daily activities are likely to require significant modification.	Promote movement and reduce impairment by improving strength and active range of motion. Promote adaptation in daily activities while incorporating the affected upper limb wherever safely possible.
None	Unlikely to regain useful movement in their hand and arm within 3 months.	Prevent secondary complications such as pain, spasticity, and shoulder instability. Reduce disability by learning to complete daily activities with the stronger hand and arm.

about what to expect for patients' upper limb recovery, evaluated with a 5-point Likert scale, as well as therapy content and duration. Therapy content was categorized during each therapy session as passive movement, strength training, and task-specific training, and any combination of these categories could be recorded for a given session (online-only Data Supplement). Therapy duration was defined as the total number of minutes spent in therapist-delivered upper limb therapy. Utilization of subsequent services was determined according to whether the patient was referred to and attended by an outpatient or community rehabilitation service.

Clinical Measures

Baseline assessments made by certified assessors 3 days poststroke included upper limb impairment (Fugl-Meyer [FM] upper extremity score),[13,14] stroke severity (National Institutes of Health Stroke Scale [NIHSS]),[15] and comorbidities (Charlson Comorbidity Index).[16] Subsequent clinical measures were obtained by trained clinical assessors who were not involved in patient care, and were blind to PREP algorithm predictions and whether the patient was in the implementation or comparison group. The primary clinical outcome was upper limb function measured with the ARAT score[17] 3 months poststroke. ARAT scores were used to determine whether patients achieved the predicted level of upper limb function (Excellent 51–57, Good 34–50, Limited 13–33, or None 0–12).[2] Secondary outcomes were upper limb impairment (FM) and pain-free passive range of motion (PROM) of the paretic shoulder 3 months poststroke, and Functional Independence Measure[18] motor subscale score on discharge from inpatient care. Follow-up outcomes 6 months poststroke were paretic upper limb use (Motor Activity Log),[19] independence (modified Rankin Scale),[20] quality of life (Stroke Impact Scale),[21] and patient satisfaction with upper limb rehabilitation and recovery (online-only Data Supplement). Variables binarized for analysis were stroke severity (mild=NIHSS score of 0–4; moderate–severe=NIHSS score of ≥5), age (<80 years, ≥80 years), comorbidities (low=Charlson Comorbidity Index score of 0 or 1; high=Charlson Comorbidity Index ≥2), and independence (independent=modified Rankin Scale score of 0, 1, 2; dependent=modified Rankin Scale score of ≥3).

Statistical Analysis

We planned to recruit 240 patients (120 per group), to produce a sample of 200 patients for analysis of inpatient length of stay. With an estimated mean length of stay of 20 days (SD=10 days), a sample of 200 patients could detect a between-group difference of 4 days, with α=0.05 and β=0.80. The effect of PREP algorithm implementation length of stay was evaluated with generalized linear modeling, with factors group, FM score, age, sex, comorbidities, and the age×sex interaction. This analysis was repeated with stroke severity instead of FM score, as these 2 predictors could not be included in the same model because of collinearity. Therapy duration was modeled with factors group, prediction category, age, sex, comorbidities, and the group×prediction category and age×sex interactions. Stroke severity was not a factor because of collinearity with prediction category. Each therapy category (passive movement, strength training, and task-specific training) was binarized as present or absent in the therapy package for each patient and analyzed for patients in each prediction category using χ^2 tests. Therapist confidence was compared between groups with a Mann–Whitney *U* test of Likert scale scores. The proportion of patients who used outpatient or community rehabilitation services was compared between groups with a χ^2 test. An independent medians test compared length of stay for all admitted stroke patients during the comparison and implementation phases of the study, obtained from the hospital's stroke database.

The percentage of patients who achieved at least their predicted level of upper limb function 3 months poststroke was compared between groups with a χ^2 test. The association between prediction categories and the primary clinical outcome was evaluated with generalized linear modeling of ARAT score 3 months poststroke. The model included factors group, prediction category, age, sex, comorbidities, and the group×prediction category and age×sex interactions. The same model was applied to the secondary outcomes of FM score and shoulder PROM 3 months poststroke. Discharge Functional Independence Measure motor subscale scores were compared between groups with a Mann–Whitney *U* test. Generalized linear modeling was used for follow-up measures 6 months poststroke (online-only Data Supplement).

Results of generalized linear modeling are reported with estimated marginal means and 95% confidence intervals. Statistical significance was set at α <0.05, and post hoc tests were 2-sided and corrected for multiple comparisons.

Results

We screened 1273 patients with stroke admitted between March 26, 2012 and October 29, 2015 (Figure 2). The PREP algorithm was suitable for 459 patients (36%). The main reasons for the algorithm being unsuitable were that the patient had no new or completely resolved upper limb motor symptoms, followed by the patient being for palliative care. Of the 459 patients for whom the PREP algorithm was suitable, 267 (58%) were unsuitable for participation in research. The main reasons were reduced capacity for informed consent, and residing out of the region precluding follow-up.

We recruited 192 patients (45% women, mean [SD] age=72 [15] years), 82 patients in the comparison phase and 110 patients in the implementation phase (Figure 2). The target sample size of 240 was not able to be recruited within the study's timeframe. Baseline characteristics were similar between groups (Table 2). The between-group difference in baseline upper limb impairment was controlled for in statistical analyses. Twenty-seven patients had initially severe impairment (SAFE score <5) but also had MEPs to

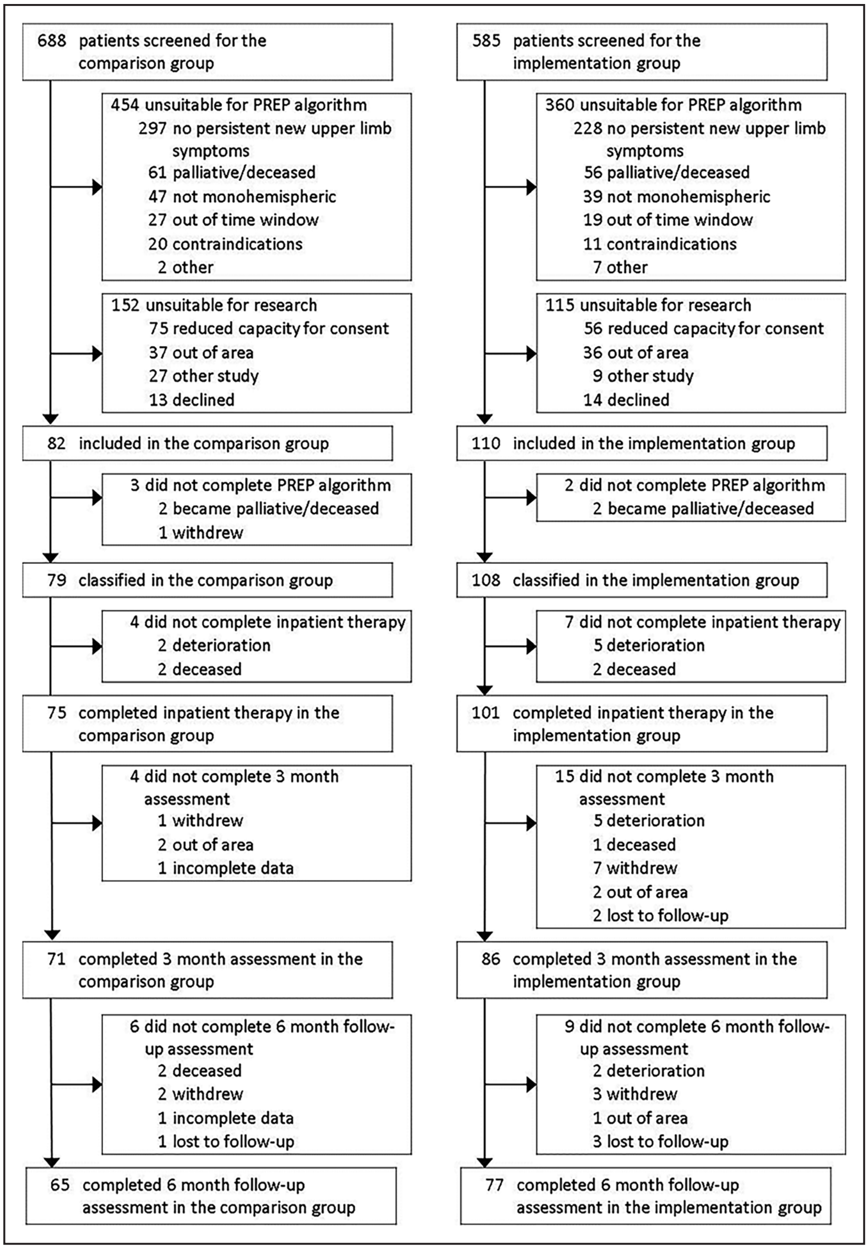

Figure 2. Study profile. PREP indicates Predict Recovery Potential.

TMS, indicating potential for a Good outcome. The study was underpowered for the Limited and None prediction categories, and these were combined to form a Poor prediction category for analysis. Adverse events affected a similar percentage of patients in both groups (comparison 16% and implementation 15%) and were unrelated to study procedures. Adverse events affecting comparison group patients were death (6), fall (3), seizure (1), recurrent stroke (1), and new cancer diagnosis (2). Adverse events affecting implementation group patients were death (5), fall (2), recurrent stroke (6), new cancer diagnosis (1), and significant cognitive decline (2).

Effects on Clinical Practice

Of the 192 patients recruited, 176 (92%) completed inpatient therapy (Figure 2). Inpatient length of stay was 1 week shorter in the implementation group, controlling for baseline FM score, age, sex, and comorbidities (Table 3). Modeling length of stay with stroke severity instead of FM score produced similar results (Table I in the online-only Data Supplement). This was not because of a shorter length of stay for all stroke patients admitted to our hospital during the implementation phase compared with the comparison phase (online-only Data Supplement; n=1758; P=0.23). Nor was the shorter length of stay associated with increased utilization of outpatient or community rehabilitation services (implementation=53%; comparison=57%; χ^2=0.41; P=0.53). As expected, length of stay was shorter for patients with less upper limb impairment.

Therapists agreed more strongly during the implementation phase with the statement "at the beginning of rehabilitation, I knew what to expect for this patient's upper limb recovery" (implementation median=4, interquartile range=1; comparison median=3, interquartile range=1; U=2564; P=0.004). PREP algorithm implementation also altered the content of

Table 2. Demographic and Baseline Clinical Characteristics

	Implementation (n=110)	Comparison (n=82)	*P* Value
Demographic characteristics			
Age, y			1.00*
<80	70 (64%)	52 (63%)	
≥80	40 (36%)	30 (37%)	
Median age (range)	72 (32–98)	74 (18–93)	0.80†
Sex			0.56*
Male	63 (57%)	43 (52%)	
Female	47 (43%)	39 (48%)	
Ethnicity			0.21‡
European	66 (60%)	51 (62%)	
Maori	5 (4%)	5 (6%)	
Pacific	14 (13%)	16 (20%)	
Asian	25 (23%)	10 (12%)	
Stroke risk factors			
Smoker	14 (13%)	8 (10%)	0.65*
Ex-smoker	22 (20%)	9 (11%)	0.11*
Diabetes mellitus	21 (19%)	23 (28%)	0.17*
Hypertension	67 (61%)	56 (68%)	0.36*
Dyslipidemia	31 (28%)	29 (35%)	0.35*
Atrial fibrillation	27 (25%)	23 (28%)	0.62*
Previous cardiac history	26 (24%)	32 (39%)	0.03*
Comorbidities (Charlson Comorbidity Index)			0.03*
Low (Charlson<2)	83 (75%)	49 (60%)	
High (Charlson≥2)	27 (25%)	33 (40%)	
Stroke characteristics			
First stroke			0.45*
Yes	88 (80%)	70 (85%)	
No	22 (20%)	12 (15%)	
Stroke type (Oxfordshire classification)			0.20‡
Total anterior circulation infarct	8 (7%)	11 (13%)	
Partial anterior circulation infarct	45 (41%)	31 (38%)	
Lacunar infarct	39 (36%)	22 (27%)	
Posterior circulation infarct (excluding cerebellar)	7 (6%)	3 (4%)	
Intracerebral hemorrhage	11 (10%)	15 (18%)	
Hemisphere			0.31*
Right	61 (55%)	39 (48%)	
Left	49 (45%)	43 (52%)	

(*Continued*)

Table 2. Continued

	Implementation (n=110)	Comparison (n=82)	*P* Value
r-tPA			0.66*
Yes	15 (14%)	9 (11%)	
Clot retrieval			0.58*
Yes	1 (1%)	2 (2%)	
Stroke severity			0.06‡
Mild (NIHSS score <5)	63 (57%)	35 (43%)	
Moderate–severe (NIHSS score ≥5)	47 (43%)	47 (57%)	
Paretic upper limb measures			
Upper limb impairment			
Fugl-Meyer UL median (max 66, range)	54.5 (2–65)	42.5 (2–65)	0.02§
PREP prediction category			0.66‡
Excellent	54 (49%)	34 (42%)	
Good	41 (37%)	31 (38%)	
Limited	7 (6%)	9 (11%)	
None	6 (6%)	5 (6%)	
Unclassified	2 (2%)	3 (3%)	

Unclassified refers to patients who did not complete the PREP algorithm, and their prognosis remained unknown (Figure 2). NIHSS indicates National Institutes of Health Stroke Scale; PREP, Predict Recovery Potential; r-tPA, recombinant tissue-type plasminogen activator; and UL, upper limb.

*Fisher exact test for 2×2 comparisons.

†Student 2-tailed *t* test.

‡Pearson χ^2 test.

§Mann–Whitney *U* test.

upper limb therapy as intended. The percentage of patients with a prediction of Excellent recovery whose upper limb therapy included passive movement was lower in the implementation group (implementation=8%; comparison=32%; χ^2=8.36; *P*=0.004). There were fewer patients in the Good prediction category in the implementation group whose therapy included strength training (implementation=64%; comparison=100%; χ^2=6.06; *P*=0.01) and passive movement (implementation=47%; comparison=70%; χ^2=3.51; *P*=0.061). The percentage of patients in the Poor prediction category whose therapy included functional tasks was also lower in the implementation group (implementation=55%; comparison=93%; χ^2=4.96; *P*=0.03). These effects demonstrate the modification of upper limb therapy content based on PREP predictions. There was a main effect of PREP prediction category on total upper limb therapy time, which was lower for patients in the Excellent category than those in the Good or Poor categories (both *P*<0.001; Table 3). PREP implementation did not affect upper limb therapy duration, which means that patients in a given prediction category completed a similar amount of upper limb therapy, regardless of whether their clinical team was aware of their category. Prediction information affected therapy content rather than duration.

Clinical Outcomes

Of the 192 patients recruited, 157 (82%) completed the primary end point at 3 months and 142 (74%) completed 6-month follow-up (Figure 2). The patients who did not complete the primary end point were more likely to have experienced a moderate–severe stroke and had higher comorbidities, although their age, stroke risk factors, and upper limb prognoses were similar to those who completed the primary end point. The PREP algorithm correctly predicted the primary clinical outcome for 80% of patients. The proportions of patients who achieved (61%) or exceeded (19%) the predicted level of upper limb function were similar between groups (χ^2=1.99; P=0.37). There was no effect of prediction category (χ^2=5.24; P=0.07) on whether patients achieved their predicted level of upper limb function.

As expected, ARAT score was highest for patients with a prediction of Excellent outcome, lower for those with a prediction of Good outcome, and lowest for those with a Poor outcome prediction (all P<0.001; Table 4). ARAT score was also higher for men and patients aged <80 years. PREP implementation did not affect the primary clinical outcome.

There were also significant differences in patients' paretic upper limb impairment according to the prediction category. Secondary outcomes of FM score and shoulder PROM were highest for patients with a prediction of Excellent outcome, lower for those with a prediction of Good outcome, and lowest for those with a Poor outcome prediction (all P<0.01; Table 4). FM score and shoulder PROM were also higher for patients aged <80 years and those with low comorbidities. Functional Independence Measure motor subscale scores on discharge were similar between groups (U=4313.5; P=0.112). PREP implementation did not affect these secondary outcomes or follow-up outcomes 6 months poststroke (online-only Data Supplement).

Discussion

This is the first study to use an algorithm combining clinical measures and biomarkers to make motor outcome predictions and guide rehabilitation decisions for individual patients. PREP algorithm implementation increased therapists' confidence and focused the content of upper limb therapy. This was associated with a 1-week reduction in inpatient length of stay. There was no change in length of stay for all stroke patients admitted to the study site hospital during the comparison and implementation phases, so the effect of PREP implementation is probably not because of a background change in policy or clinical practice. The shortened length of stay did not come at the expense of clinical outcomes, with no detrimental effects of PREP implementation on primary, secondary, or follow-up outcomes, and no increase in the utilization of outpatient rehabilitation services. The use of an algorithm to predict recovery potential for individual patients can, therefore, increase rehabilitation efficiency after stroke without compromising clinical outcome. Although implementation of the PREP algorithm did not improve outcomes in the context of current therapy practice, guiding rehabilitation with predictive information seems to help patients leave hospital sooner.

The effects of predictive information on therapist and patient expectations and behavior may be key factors contributing to shortened length of stay. PREP algorithm information increased therapist confidence, which is perhaps unsurprising. However, it is useful to confirm that the information did influence therapists' perceptions and was not distrusted or disregarded. Therapists were provided with a prediction of likely outcome and rehabilitation focus for each patient, and they remained free to select treatments from the

Table 3. Generalized Linear Modeling of Clinical Practice Measures

	Estimated Marginal Mean	95% CI	Wald χ^2	*P* Value
Length of stay, d				
FM score			171.35	<0.001
Group				
Implementation	11	9–13	11.12	0.001
Comparison	17	14–21		
Age				
<80 y	12	10–15	3.50	0.06
≥80 y	16	13–19		
Sex				
Male	15	12–18	0.01	0.95
Female	13	11–16		
Comorbidities				
Low	14	12–17	0.18	0.67
High	14	11–17		
Age×sex			0.59	0.44
Upper limb therapy dose, min				
Prediction				
Excellent	19	14–27	81.84	<0.001
Good	139	97–198		
Poor	147	82–263		
Group				
Implementation	63	44–91	1.56	0.21
Control	85	60–122		
Age				
<80 y	83	61–112	1.02	0.31
≥80 y	65	44–97		
Sex				
Male	83	57–121	1.14	0.29
Female	65	47–90		
Comorbidities				
Low	61	45–83	2.242	0.13
High	88	59–131		
Group×prediction			4.20	0.12
Age×sex			0.13	0.72

Poor=Limited and None prediction categories combined. CI indicates confidence interval; and FM, Fugl-Meyer.

Table 4. Generalized Linear Modeling of Clinical Outcomes 3 Months Poststroke

	Estimated Marginal Mean	95% CI	Wald χ^2	*P* Value
Primary clinical outcome: ARAT score				
Prediction				
Excellent	53	51–55	407.63	<0.001
Good	45	42–47		
Poor	9	5–13		
Group				
Implementation	36	33–38	0.03	0.85
Comparison	35	33–38		
Age				
<80 y	37	36–39	6.91	0.009
≥80 y	34	31–36		
Sex				
Male	37	35–40	6.16	0.01
Female	34	32–36		
Comorbidities				
Low	37	35–39	2.83	0.09
High	34	32–37		
Group×prediction			1.48	0.48
Age×sex			1.19	0.28
Secondary clinical outcome: FM score				
Prediction				
Excellent	62	59–64	387.96	<0.001
Good	53	50–55		
Poor	19	15–23		
Group				
Implementation	44	41–46	1.12	0.29
Comparison	45	43–47		
Age				
<80 y	46	44–48	4.00	0.045
≥80 y	43	40–45		
Sex				
Male	46	43–48	3.53	0.06
Female	43	41–45		
Comorbidities				
Low	46	44–48	4.87	0.03
High	43	40–45		
Group×prediction			3.32	0.19
Age×sex			0.90	0.34
Secondary clinical outcome: shoulder PROM (degrees)				
Prediction				
Excellent	336	322–349	75.88	<0.001
Good	302	288–316		
Poor	217	194–241		
Group				
Implementation	284	269–299	0.08	0.77
Comparison	286	273–300		
Age				
<80 y	295	282–307	4.25	0.039
≥80 y	275	260–291		
Sex				
Male	288	273–303	0.53	0.47
Female	282	269–295		
Comorbidities				
Low	297	284–309	6.04	0.01
High	273	257–289		
Group×prediction			4.82	0.09
Age×sex			2.62	0.11

Poor=Limited and None prediction categories combined. ARAT indicates Action Research Arm Test; CI, confidence interval; FM, Fugl-Meyer; and PROM, passive range of motion.

standard care repertoire. Therapists responded by modifying therapy content appropriately. Patients were also provided with a description of the minimum level of upper limb function that they could expect to achieve within 3 months. This may have enhanced their motivation to engage with therapist-directed and self-directed practice. These combined factors may have helped patients in the implementation group to recover more quickly, enabling earlier discharge. This could be explored in future studies by including measures of patient motivation and self-directed practice. Although algorithm predictions modified therapy content, this had no effect on final upper limb outcomes, in keeping with recent multicenter trials.[22–24] Algorithm predictions may be useful for selection and stratification of patients in future trials of novel treatments. In the meantime, it seems that PREP algorithm information can improve the efficiency of current rehabilitation practice.

Experienced clinicians find it difficult to accurately predict motor outcomes after stroke.[25] In general, patients with less initial motor impairment,[3] and less damage to the corticomotor system,[4] have better motor outcomes. However, these relationships have been demonstrated for groups of patients, often in regression models that are not always useful when providing prognoses to patients. The PREP algorithm represents a new approach, where clinical measures and biomarkers are used to make predictions for individual patients and focus rehabilitation accordingly. This may be particularly important for patients such as those in this study with severe initial motor impairment and a functionally intact corticospinal tract (n=27). Without biomarker information about the corticospinal tract, the potential for a Good recovery of function by patients such as these might go unrecognized by clinicians planning rehabilitation.

The PREP algorithm correctly predicted the primary clinical outcome in 80% of patients, consistent with the training data set.[2] However, further work is needed to improve its accuracy, with the goal of predicting the exact rather than minimum expected level of recovery. A detailed analysis of the algorithm's performance will be reported separately. This study validates the algorithm in a larger, more heterogeneous sample of patients, by confirming large effects of PREP prediction category on upper limb function. It also demonstrates for the first time large effects of PREP prediction category on upper limb impairment 3 months poststroke and upper limb use in daily activities 6 months poststroke. Similar proportions of patients in both groups achieved and exceeded the predicted level of upper limb function, allaying concerns that providing predictions may create self-fulfilling prophecies that limit recovery.

The majority of patients had mild or moderate stroke, and outcomes were influenced as expected by stroke severity,[26,27] age,[26–29] sex,[28–30] and comorbidities.[29] The study was underpowered to separately detect effects on patients in the Limited or None categories, and further testing of the PREP algorithm with patients in these categories is needed. Another limitation was the use of a sequential rather than randomized study design. It is possible that the reduced length of stay was because of factors other than predictive information affecting expectations and clinical practice during the implementation phase. However, length of stay for all stroke patients admitted to our hospital was stable throughout the study, indicating that the reduced length of stay was only experienced by patients recruited to the implementation group. A future multicenter study could randomize sites to recruit for either the comparison or implementation arm of the study. Strengths of the study include broad inclusion criteria, and implementation of the PREP algorithm in a real-world rehabilitation setting with clinical staff involved in obtaining and using prognoses. The PREP algorithm was suitable for 36% of patients screened, which compares favorably with rehabilitation interventions.[31] A prediction was made for 133 patients (69%) using only the SAFE score, and therapists were trained to obtain TMS measures. These features support translation to clinical practice.

Conclusions

This study demonstrates for the first time that prediction algorithms can be used to guide clinical decision-making for individual stroke rehabilitation patients. This proof of concept opens the door to using such algorithms in stroke rehabilitation practice, and exploring their potential for predicting outcomes in other functional domains such as communication or cognition. Providing objective predictions can focus rehabilitation and help patients leave hospital sooner.

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