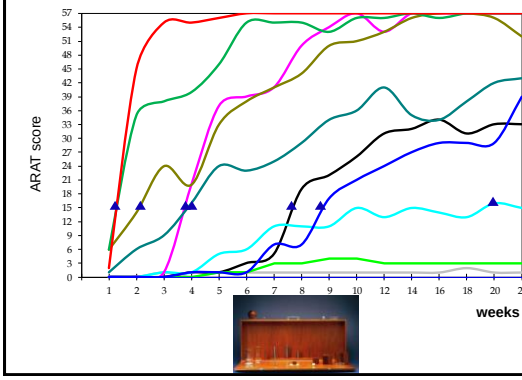
VOORSPELLEN VAN FUNCTIONEEL HERSTEL VAN ARM-HANDVAARDIGHEID: WAAR MOET IK OP LETTEN?

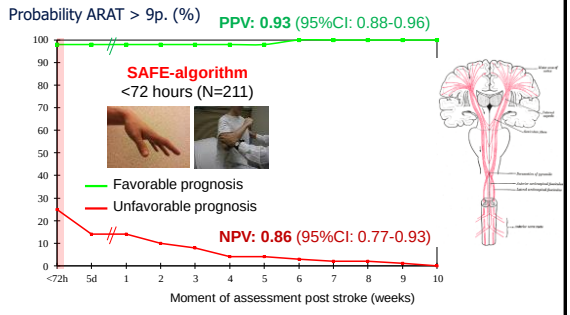
Prof. Gert Kwakkel
Chair Neurorehabilitation,
VU University Medical Center, Amsterdam
(g.kwakkel@vumc.nl)

Neuroscience Campus Amsterdam

Predicting upper limb recovery (N=10)



Predicting upper limb recovery (N=211)



Nijland et al, Stroke. 2010;41:745-50
Stinear et al, Lancet Neurol 2010; Dec;9(12):1228-32

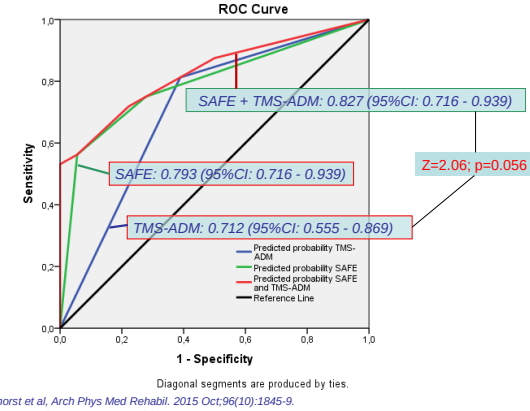
*What is the **added value** of TMS-induced MEPs clinical above clinical modelling very early post stroke?*

Hoonhorst et al, Arch Phys Med Rehabil. 2015 Oct;96(10):1845-9.
Hoonhorst et al, Neurorehabil Neural Repair. 2018 Aug;32(8):682-690.

Predictive validity of SAFE model and TMS-MEP for recovery of dexterity at 6 months using FMA ≥ 22 points as cut-off score (N=51)

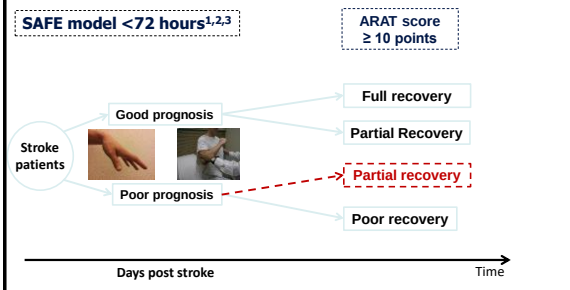
	Clinical observation by SAFE (95%CI) < 48 hours	TMS ADM-MEP (95%CI) < 48 hours
PPV :	**0.95 (95%CI: 0.76–0.99)**	**0.79 (95%CI: 0.68 - 0.88)**
NPV:	**0.55 (95%CI: 0.44 – 0.58)**	**0.65 (95%CI: 0.43 - 0.82)**

Hoonhorst et al, Arch Phys Med Rehabil. 2015 Oct;96(10):1845-9.
Hoonhorst et al, Neurorehabil Neural Repair. 2018 Aug;32(8):682-690.



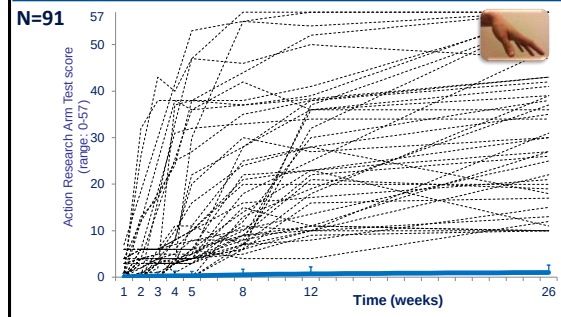
Hoonhorst et al, Arch Phys Med Rehabil. 2015 Oct;96(10):1845-9.
Hoonhorst et al NNR 2018 Aug;32(8):682-690.

Prognosis for recovery of upper limb capacity within the first days post stroke



[1] Nijland et al. Stroke 2010;41(4):745-750;
[2] Stinear et al. Lancet Neurol 2010;9:1228-1232;
[3] Winters et al. Plos One 2016 Aug 5; 11(8): e0160528

Spontaneous return of finger extension: Prognosis for early return recovery of upper limb capacity

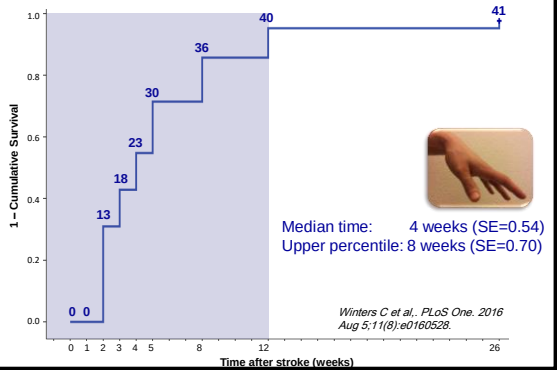


Winters et al. Plos One 2016 Aug 5; 11(8): e0160528

False negatives at 6 months: ARAT ≥ 10 points (N=42)
True negatives at 6 months: ARAT < 10 points (N=49)

Kaplan-Meyer curve for return of voluntary finger extension

False negatives at 6 months: ARAT ≥ 10 points (N=42)



Median time: 4 weeks (SE=0.54)
Upper percentile: 8 weeks (SE=0.70)

Winters C et al., PLoS One. 2016 Aug 5;11(8):e0160528.

Prognosis for regaining upper limb capacity (N=91)

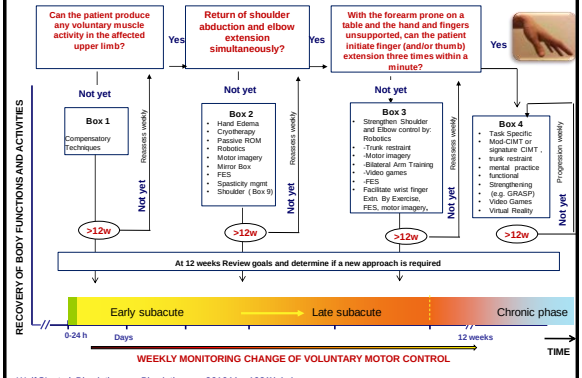
LOWER LIMB MOTOR FUNCTION (MI)	VISUOSPATIAL NEGLECT (LCT)	SOMATOSENSORY DEFICIT (EmNSA)	Predicted probability
Good	No	No	0.94
Poor	Yes	Yes	0.04

True negatives
False negatives

MI: Motricity Index leg, cutoff: 35 points;
LCT: Letter Cancellation Test, cutoff: asymmetry 2 points;
EmNSA: Erasmus MC modified Nottingham Sensory Assessment, cutoff 33 points.

Winters C et al, PLoS One. 2016 Aug 5;11(8):e0160528.

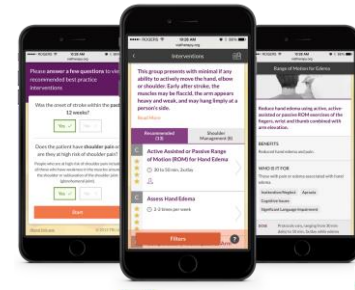
Prognostic algorithm for upper limb rehabilitation



Wolf SL et al, Physiotherapy. Physiotherapy. 2016 Mar;102(1):1-4.

Stroke Rehab App.: http://www.viatherapy.org/

Wolf SL et al, Physiotherapy. Physiotherapy. 2016 Mar;102(1):1-4.

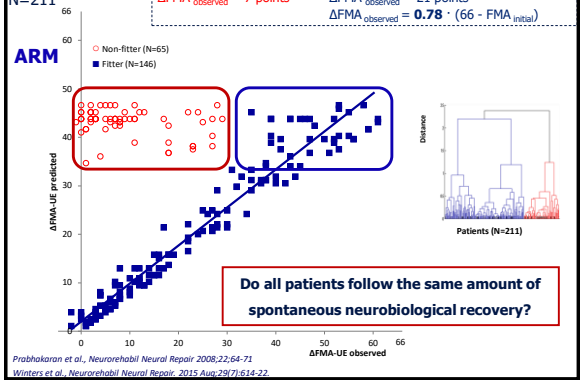


UHN Toronto General Toronto Western Princess Margaret Toronto Rehab
University of South Australia
EMORY UNIVERSITY
VUmc
Reade revalidatie | reumatologie
VU University Medical Center Amsterdam

EPOS cohort study < 72 hours N=211

Non-fitters: N=65
$\Delta FMA_{predicted}$ = 44 points
$\Delta FMA_{observed}$ = 7 points

Fitters: N=146
$\Delta FMA_{predicted}$ = 18 points
$\Delta FMA_{observed}$ = 21 points
$\Delta FMA_{observed}$ = **0.78** · (66 - $FMA_{initial}$)



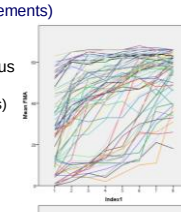
Do all patients follow the same amount of spontaneous neurobiological recovery?

Prabhakaran et al., Neurorehabil Neural Repair 2008;22;64-71
Winters et al., Neurorehabil Neural Repair. 2015 Aug;29(7):614-22.

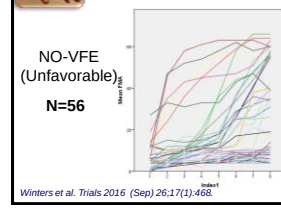
Proportional recovery rule following the FM-arm score (N=112; i.e., 896 measurements)

VFE onset (Favorable)
N=56

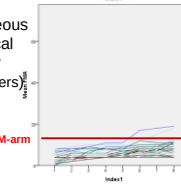
Showing spontaneous recovery (i.e., Fitters)
N=81



NO-VFE (Unfavorable)
N=56



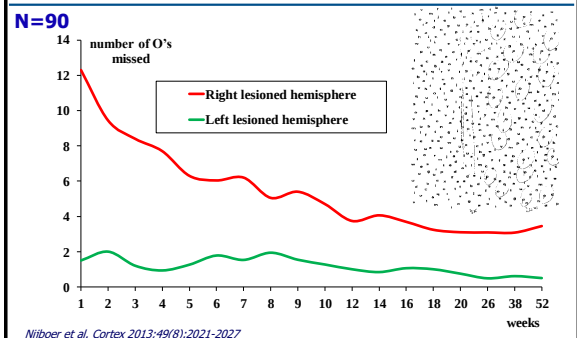
No spontaneous neurological recovery (i..e, Non-Fitters)
N=31



Winters et al. Trials 2016 (Sep) 26;17(1):468.

Is the proportional recovery rule also generalizable to visuospatial neglect early poststroke?

N=90



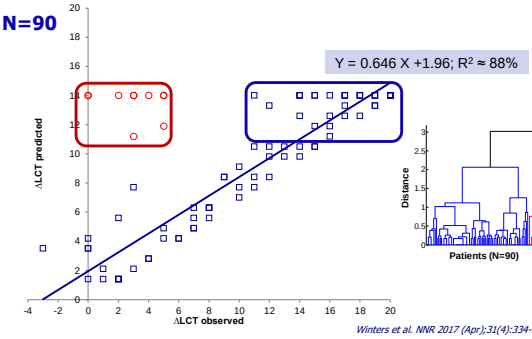
Nijboer et al. Cortex 2013;49(8):2021-2027
Winters et al, Neurorehabilitation and Neural Repair 2017 (Apr); 31(4):334-342.

Non-fitters: N=11
$\Delta LCT_{predicted}$ = 13.5 (± 1.1 p.)
$\Delta LCT_{observed}$ = 3.0 (± 1.9 p.)

Fitters: N=79
$\Delta LCT_{predicted}$ = 9.28 (± 4.5 p.)
$\Delta LCT_{observed}$ = 11.3 (± 6.5 p.)
$\Delta LCT_{observed}$ ≈ **0.81** x (20 - $LCT_{initial}$)

N=90

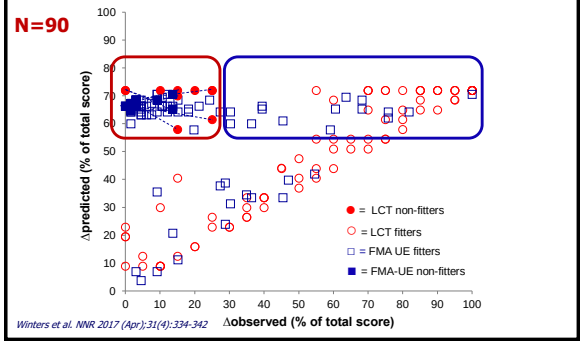
Y = 0.646 X +1.96; R^2 ≈ 88%



Winters et al. NNR 2017 (Apr);31(4):334-342.

Identification of fitters and non-fitters with respect to the 'proportional recovery rule' of motor recovery of the left upper paretic limb compared to those with visual inattention (expressed in %) measured in patients with a first-ever, ischemic **right**-hemispheric stroke lesion.

N=90



Winters et al. NNR 2017 (Apr);31(4):334-342

Improving the proportional recovery rule for FM-arm scores by using Markow Chain Monte Carlo methods (MCMC)

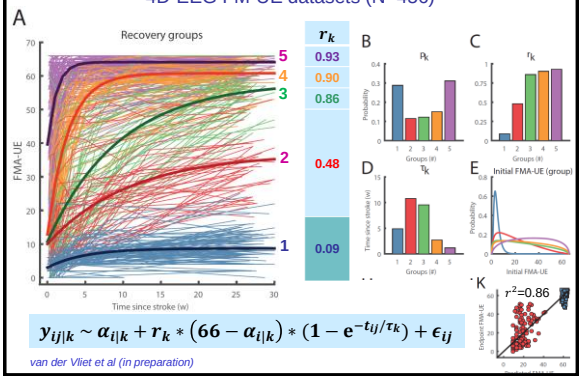
$$y_{ij|k} \sim \alpha_{i|k} + r_k * (66 - \alpha_{i|k}) * (1 - e^{-t_{ij}/\tau_k}) + \epsilon_{ij}$$

i = patient identification number $[1\ I]$
j = measurement identification number $[1\ J]$
k = subpopulation (cluster) identification number $[1\ k]$
$y_{ij|k}$ = FMA-UE for patient i and measurement j nested in subgroup K $[0 - 66]$
$\alpha_{i|k}$ = patient i specific intercept nested within subgroup k $[0 - 66]$
r_k = recovery coefficient for each subgroup k $[0 - 1]$
t_{ij} = individual time course post stroke
τ_k = time constant for subgroup k in weeks $[0 - \infty]$
ϵ_{ij} = model error for patient i at time point j

$\alpha_i \sim B(\gamma_{\alpha,k}, \delta_{\alpha,k})$
$\gamma_{\alpha,k} \sim \Gamma(10^{-3}, 10^{-3})$
$\delta_{\alpha,k} \sim \Gamma(10^{-3}, 10^{-3})$
$r_k \sim U(0,1)$
$k \sim Cat(K, P), P \sim Dir(10^{-5})$
$\tau_k \sim \Gamma(10^{-3}, 10^{-3})$
$\epsilon_{ij} \sim N(0, \sigma_\epsilon^2), \sigma_\epsilon \sim U(0,100)$

van der Vliet et al, (in preparation)

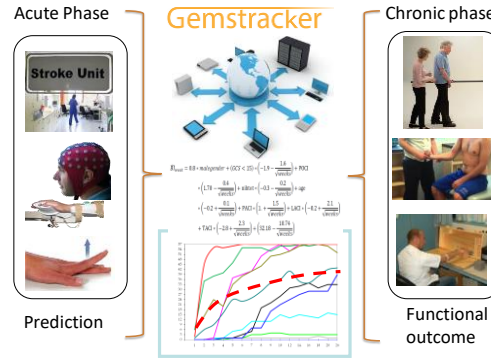
Applying MCMC (mixture) methods on the EXPLICIT, EPOS and 4D-EEG FM-UE datasets (N=456)



$$y_{ij|k} \sim \alpha_{i|k} + r_k * (66 - \alpha_{i|k}) * (1 - e^{-t_{ij}/\tau_k}) + \epsilon_{ij}$$

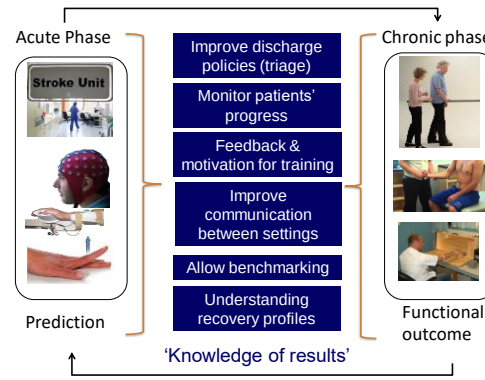
van der Vliet et al (in preparation)

Web-based ICT-solutions for patient-specific predictions

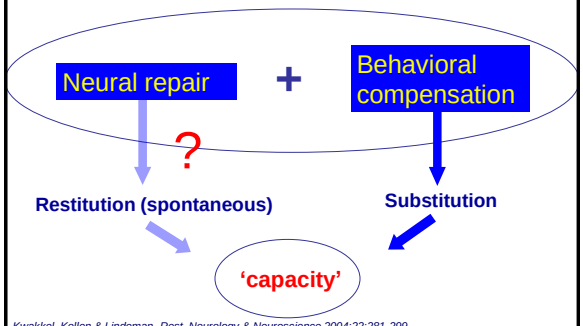


Immediate visualization of patient-specific prognosis based on mixture methods

Individualized patient-specific prediction modeling



Understanding functional improvements….



Kwakkel, Kollen & Lindeman, Rest. Neurology & Neuroscience 2004;22:281-299
Buma et al, Rest Neurol Neuroscience 2013; 31(6):707-722)

How to improve stroke recovery and rehabilitation trials?


Guidelines

International Journal of Stroke WSO

Moving rehabilitation research forward: Developing consensus statements for rehabilitation and recovery research

Julie Bernhardt[1,2], Karen Borschmann[1,2], Lara Boyd[3], S Thomas Carmichael[4], Dale Corbett[5,6], Steven C Cramer[7], Tammy Hoffmann[8], Gert Kwakkel[9], Sean I Savitz[10], Gustavo Saposnik[11,12], Marion Walker[13] and Nick Ward[14,15]

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Consensus

Consensus

Consensus

Consensus

Consensus

Standardized measurement of sensorimotor recovery in stroke trials: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable

Gert Kwakkel[1], Natasha A Lannin[2], Karen Borschmann[3], Coralie English[4], Myzoon Ali[5], Leonid Churilov[3], Gustavo Saposnik[6], Carolee Winstein[7], Erwin EH van Wegen[8], Steven L Wolf[9], John W Krakauer[10] and Julie Bernhardt[3]

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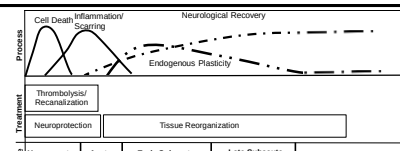

Dobkin BH, Carmichael ST. Neurorehabil Neural Repair. 2016 Jun;30(5):470-8.

CORE SET OF OUTCOMES AT FIXED TIMES POST STROKE

< 72 hours	Acute	Early Subacute at 7 days	Late Subacute at 3 months	Chronic
NIHSS	NIHSS		NIHSS at 3 months (Descriptor)	NIHSS (descriptor) at 3 m. (Descriptor)
FM-motor	FM-motor score	FM-motor score	FM-motor score	FM-motor score
	ARAT	ARAT	ARAT	ARAT
		Biomechanics	**Biomechanics**	**Biomechanics**
	Can you walk 10m? FAC	Can you walk 10m? FAC	Can you walk 10m? FAC	Can you walk 10m? FAC
		mRS (3 months)	mRS	mRS
		EQ-5D (3 months)	EQ-5D	EQ-5D

Dank voor uw aandacht!

DSNR
Dutch Society of Neuro-Rehabilitation

www.neurorehab.nl

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