Supplementary Online Content

Galovic M, Stauber AJ, Leisi N, et al. Development and validation of a prognostic model of swallowing recovery and enteral tube feeding after ischemic stroke: Predictive Swallowing Score. *JAMA Neurol*. Published online February 11, 2019. doi:10.1001/jamaneurol.2018.4858

This supplementary material has been provided by the authors to give readers additional information about their work.
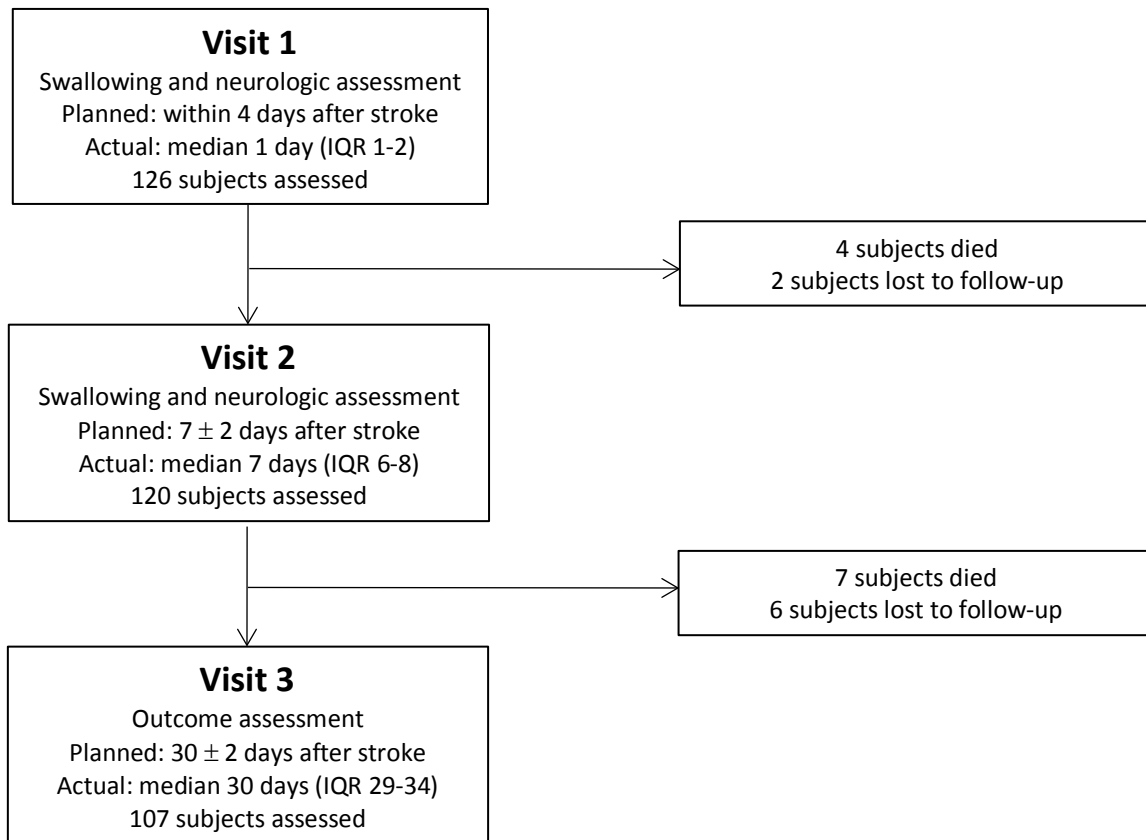
1. Study Flow Charts

1.1 Study flow chart in derivation cohort

*follow-up visits were only performed if the subject was not recovered (FOIS < 5) at the previous evaluation.

Visit 1
Swallowing and neurologic assessment
Planned: within 4 days after stroke
Actual: median 1 day (IQR 1-2)
153 subjects assessed

Daily follow up
Regular swallowing assessment by SLT
20 subjects recovered
0 subjects lost to follow-up
1 subject died

Visit 2
Swallowing assessment
Planned: 7 ± 2 days after stroke
Actual: median 8 days (IQR 7-9)
132 subjects assessed

Daily follow up
Regular swallowing assessment by SLT
23 subjects recovered
2 subjects lost to follow-up
0 subjects died

Visit at discharge
Swallowing and neurologic assessment
Planned: at discharge
Actual: median 12 days (IQR 6-17)
107 subjects assessed

7 subjects recovered
56 subjects lost to follow-up
5 subjects died

Visit 3
Outcome assessment
Planned: > 30 days after stroke
Actual: median 37 days (IQR 33-43)
39 subjects assessed

1.2 Study flow chart in validation cohort

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1.2 Study flow chart in validation cohort

Visit 1
Swallowing and neurologic assessment
Planned: within 4 days after stroke
Actual: median 1 day (IQR 1-2)
126 subjects assessed

→ 4 subjects died
2 subjects lost to follow-up

Visit 2
Swallowing and neurologic assessment
Planned: 7 ± 2 days after stroke
Actual: median 7 days (IQR 6-8)
120 subjects assessed

→ 7 subjects died
6 subjects lost to follow-up

Visit 3
Outcome assessment
Planned: 30 ± 2 days after stroke
Actual: median 30 days (IQR 29-34)
107 subjects assessed

2 Swallowing assessments

We evaluated swallowing in the derivation and validation cohorts as previously described by our group (Galovic *et al.*, 2017).

Swallowing assessment consisted of the examination of oral musculature strength, agility, and symmetry, as well as examination of protective reflexes and sensation by a speech-language pathologist. Testing included the 50 mL water swallow test (DePippo *et al.*, 1992) and Any 2 scale (Daniels *et al.*, 1997) for risk of aspiration. In the validation cohort, severity of dysphagia was quantified with the Parramatta Hospitals Assessment of Dysphagia (Broadley *et al.*, 2005) and Gugging Swallowing Screen (Trapl *et al.*, 2007). Instrumental testing with fiberoptic endoscopy or videofluoroscopy was performed in subjects with indeterminate results of the clinical evaluation or when deemed necessary by the treating physician.

We scored the severity of impaired oral intake according to the Functional Oral Intake Scale (FOIS), a widely used, reliable and valid outcome measure to document a person's safe and adequate functional oral intake (Crary *et al.*, 2005). The scale ranges from 1 (nothing by mouth) to 7 (total oral diet with no restrictions). The evaluation is based on the level of oral intake or food and liquid consistency recommended by an objective swallow evaluation. To increase generalizability, a standardized guideline was established (**Supplementary Table I**) and was previously used by our group (Galovic *et al.*, 2017). The main aspect of this guideline is the type and number of consistencies (solids, semisolids, liquids) that can be safely swallowed based on the results of clinical/instrumental testing.

The follow-up after 30 days was performed centrally via telephone by a speech-language pathologist blinded to results of previous assessments. In order to determine the current level of oral intake recommended by objective swallowing evaluations, we interviewed the stroke survivor and/or relatives and, where available, medical staff. The interview included questions on the current diet modification, return to prestroke diet, restrictions on safe food and liquid consistencies, food preparations, compensation strategies, quantity of oral intake and enteral tube feeding.

2.1 Other assessments

Stroke outcome was evaluated in the derivation cohort at discharge and in the validation cohorts at the follow-up visit after 30 days. Pneumonia was defined as $\geq$ 3 of the following: fever >38°C; productive cough; abnormal respiratory examination (tachypnoea >22 bpm, tachycardia, inspiratory crackles, bronchial breathing); culture of relevant pathogen; positive chest radiograph; and elevated CRP in a person with suspected chest infection. Dependency was scored with the modified Rankin Scale (mRS). Institutionalisation was defined as failure to return home or to an unsupported living environment. We also collected data on mortality and weight change.

2.2 References

Broadley S, Cheek A, Salonikis S, Whitham E, Chong V, Cardone D, et al. Predicting prolonged dysphagia in acute stroke: the Royal Adelaide Prognostic Index for Dysphagic Stroke (RAPIDS). Dysphagia 2005; 20: 303-310.

Crary MA, Mann GDC, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil 2005; 86: 1516-1520.

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DePippo KL, Holas MA, Reding MJ. Validation of the 3-oz water swallow test for aspiration following stroke. Arch Neurol 1992; 49: 1259-1261.

Galovic M, Leisi N, Pastore-Wapp M, Zbinden M, Vos SB, Mueller M, et al. Diverging lesion and connectivity patterns influence early and late swallowing recovery after hemispheric stroke. Hum Brain Mapp 2017; 38: 2165-2176.

Trapl M, Enderle P, Nowotny M, Teuschl Y, Matz K, Dachenhausen A, et al. Dysphagia bedside screening for acute-stroke patients: the Gugging Swallowing Screen. 2007; 38: 2948-2952.

Warnecke T, Ritter MA, Kr ouml ger B, Oelenberg S, Teismann I, Heuschmann PU, et al. Fiberoptic Endoscopic Dysphagia Severity Scale Predicts Outcome after Acute Stroke. Cerebrovasc Dis 2009; 28: 283-289.

Supplementary Table I: Guideline for Functional Oral Intake (FOIS) scoring based on a comprehensive swallow evaluation. Based on Galovic et al., 2017.

FOIS level	Safe swallowing possible for			Quantity of oral intake	Supportive findings
	semisolids	liquids	solids		
Level 7	Yes	Yes	Yes	Normal portion	• 50ml water swallow test negative • Any 2 < 2 • PHAD > 90 • GUSS = 20 • FEDSS = 1
Level 6	Yes Yes Yes Avoid challenging consistencies (e.g. mixed consistencies, crumby food)			Normal portion	• 50ml water swallow test negative • Any 2 < 2
Level 5	At least two consistencies can be swallowed securely			Normal portion	• PHAD ≤ 90 • GUSS 15 to 19 • FEDSS = 2
Level 4	Yes	No	No	Normal portion	
Level 3	Yes	No	No	≤ 50% of normal portion	• 50ml water swallow test positive • Any 2 ≥ 2 • PHAD ≤ 80 • GUSS 10 to 14 • FEDSS 3-4
Level 2	Yes	No	No	Only few spoons or sips per mouth	
Level 1	No	No	No	Nothing by mouth	• 50ml water swallow test positive • Any 2 ≥ 2 • PHAD ≤ 80 • GUSS ≤ 9 • FEDSS ≥ 4

"Safe swallowing" corresponds to consistencies that can be safely swallowed by a subject based on the results of the clinical/instrumental swallowing evaluation. "Portion" corresponds to the percent of required intake that is safely consumed by mouth.
Any 2 = Any 2 scale (Daniels *et al.*, 1997), PHAD = Parramatta Hospitals Assessment of Dysphagia (Broadley *et al.*, 2005), GUSS = Gugging Swallowing Screen (Trapl *et al.*, 2007), FEDSS = Fiberoptic Endoscopic Dysphagia Severity Scale (Warnecke *et al.*, 2009).

3. Prognostic Model of Time to Recovery of Functional Oral Intake

Variable	β	aHR (95% CI)	P Value	ΔAIC
Initial impairment of oral intake (FOIS)	−0.87	0.42 (0.31 to 0.58)	<.001	−27.1
Lesion of the frontal operculum	−0.71	0.49 (0.30 to 0.81)	.005	−6.1
Initial risk of aspiration (Any 2 test)	−0.51	0.60 (0.42 to 0.87)	.007	−5.7
Age ≥70 y	−0.56	0.57 (0.35 to 0.93)	.03	−2.8
NIHSS at admission	−0.30	0.74 (0.56 to 0.97)	.03	−2.6
Small-vessel occlusion	Eliminated in step 6		.12	−0.2
Aphasia	Eliminated in step 5		.20,	0.3
Stroke size	Eliminated in step 4		.32,	1.0
Loss of consciousness	Eliminated in step 3		.41,	1.
Bilateral infarction	Eliminated in step 2		.58	1.7
50 ml water swallow test	Eliminated in step 1		.71	1.9

N = 153.

Abbreviations: aHR, adjusted hazards ratio; FOIS, Functional Oral Intake Scale; NIHSS, NIH Stroke Scale, ΔAIC, change in Akaike Information Criterion - a factor improves the model of ΔAIC is negative

4 Missing data

Data was available for all outcome parameters and for 99% of the clinical variables. A detailed breakdown is displayed in **Supplementary Table II**. There was no other missing data. Analysis was performed using available data.

Supplementary Table II: Missing data per cohort.

Variable	Derivation cohort (n=153)	Internal validation cohort (n=)	External validation cohort (n=62)
Sex			
Male			
Female			
Age *(years)*			
Dependency *(mRS)* before admission		1	
Stroke severity *(NIHSS)* at admission			
Stroke laterality			
Left			
Right			
Bilateral			
Stroke location			
Cortical			
Subcortical			
Cerebellar			
Brainstem			
Affected arterial territory			
Middle cerebral artery			
Anterior cerebral artery			
Posterior cerebral artery			
Basilar artery			
Vertebral artery			
Thrombolysis			
Stroke etiology			
Small-vessel occlusion			
Large-artery atherosclerosis			
Cardioembolism			
Other determined origin			
Undetermined etiology			
Initial swallowing evaluation			
FOIS			
Positive 50ml water swallow test			
Any2 test			
GUSS	not performed		
PHAD	not performed	1	18
PRESS			
PEG-Score			
Stroke outcome at 30 days or at discharge			
Dependency *(mRS)*	29	4	8
Institutionalisation		8	8
Pneumonia			
Death			

mRS = modified Rankin Scale, NIHSS = NIH Stroke Scale, FOIS = Functional Oral Intake Scale, GUSS = Gugging Swallowing Screen, PHAD = Parramatta Hospitals' Assessment of Dysphagia, PRESS = Predictive Swallowing Score.

5 Univariable analysis in derivation cohort

Because previous literature does not provide sufficient data for an evidence-driven choice of predictors, we have additionally performed a univariable analysis with Cox proportional hazards regression within the derivation cohort (**Supplementary Table III**). We sought to identify factors that are associated with dysphagia recovery and have not been reported in previous studies, e.g. the degree of initial swallowing impairment, stroke aetiology, or initial clinical symptoms.

Supplementary Table III: *Univariable analysis of predictors of time to recovery of functional oral intake.*

Variable	HR (95% CI)	P value
Sex		
Male	0.88 (0.56-1.38)	0.59
Female	1.13 (0.72-1.77)	0.59
Age*	0.98 (0.96-0.995)	**0.01**
NIHSS at admission*	0.95 (0.92-0.98)	**0.002**
Clinical symptoms according to NIHSS at admission		
Loss of Consciousness	0.55 (0.38-0.81)	**0.002**
Facial Palsy	0.87 (0.67-1.1)	0.32
Language/Aphasia	0.77 (0.64-0.93)	**0.007**
Speech/Dysarthria	1.0 (0.75-1.36)	0.94
Thrombolysis	0.92 (0.59-1.43)	0.70
Instrumentation	0.68 (0.4-1.16)	0.16
Stroke etiology		
Small-vessel occlusion	3.23 (1.59-6.55)	**0.001**
Large-artery atherosclerosis	1.2 (0.7-2.1)	0.48
Cardioembolism	0.76 (0.48-1.19)	0.23
Other determined origin	1.6 (0.6-4.6)	0.32
Undetermined etiology	0.63 (0.33-1.2)	0.16
Stroke size (ASPECTS)	1.13 (1.04-1.24)	**0.007**
Lesion side		
Left	1.12 (0.70-1.76)	0.67
Right	1.12 (0.71-1.73)	0.66
Bilateral*	1.45 (0.81-2.60)	0.21
Arterial territory		
MCA	0.89 (0.50-1.59)	0.69
ACA	1.10 (0.55-2.20)	0.79
PCA	1.49 (0.80-2.76)	0.21
BA	0.69 (0.30-1.59)	0.39
VA	0.96 (0.35-2.64)	0.94
Lesion location general		
Cortical	0.80 (0.47-1.38)	0.43
Subcortical	1.04 (0.62-1.74)	0.89
Cerebellar	1.65 (0.89-3.06)	0.11
Brainstem	0.90 (0.45-1.81)	0.76
Lesion location lobar		
Frontal	0.80 (0.49-1.30)	0.37
Parietal	0.80 (0.51-1.25)	0.33
Temporal	0.67 (0.43-1.05)	0.08
Occipital	1.37 (0.72-2.61)	0.33
Lesion location cortical		
Caudal primary sensorimotor and premotor cortex	0.66 (0.41-1.04)	0.08
Insular cortex	0.68 (0.43-1.06)	0.09
Frontal operculum*	0.53 (0.33-0.85)	**0.008**
Superior temporal cortex	0.73 (0.46-1.15)	0.17
Lesion location subcortical		
Internal capsule	0.91 (0.56-1.49)	0.71
Basal ganglia	0.79 (0.50-1.25)	0.31
Periventricular white matter	0.63 (0.40-1.02)	0.06
Thalamus	0.76 (0.28-2.08)	0.59
Lesion location brainstem		
Midbrain	0.05 (0.0-0.73)	0.68
Pons	1.55 (0.74-3.24)	0.24
Lateral medulla	0.62 (0.20-1.98)	0.42
Medial medulla	No cases	-
Initial swallowing evaluation		
Initial 50ml water test	0.32 (0.14-0.75)	**0.009**
Initial risk of aspiration (Any 2 scale)*	0.63 (0.53-0.74)	**<0.001**

|		
Initial impairment of oral intake (FOIS)	1.89 (1.55-2.31)	**<0.001**

* Predictors reported in previous literature. N=153. HR = hazards ratio, CI = confidence interval, NIHSS = NIH Stroke Scale, MCA = middle cerebral artery, ACA = anterior cerebral artery, PCA = posterior cerebral artery, BA= basilar artery, VA= vertebral artery, FOIS = Functional Oral Intake Scale.

6 Calibration plots for PRESS

Calibration, i.e. the agreement between predicted and observed risks, was assessed with calibration plots for day 7 and day 30. Significant over- or underprediction is observed when a data point's 95% confidence intervals do not cross the diagonal line or when the Hosmer-Lemeshow test produces significant results. We have also estimated slopes of calibration regression lines on this plot, whereas a slope close to 1.0 (i.e. a 45-degree diagonal line) reflects perfect calibration.

Supplementary Figure I: *Calibration plots for a previously proposed model of PEG placement (PEG score).*
Diagonal line indicates perfect calibration. Vertical bars show 95% confidence intervals. HL=Hosmer-Lemeshow.
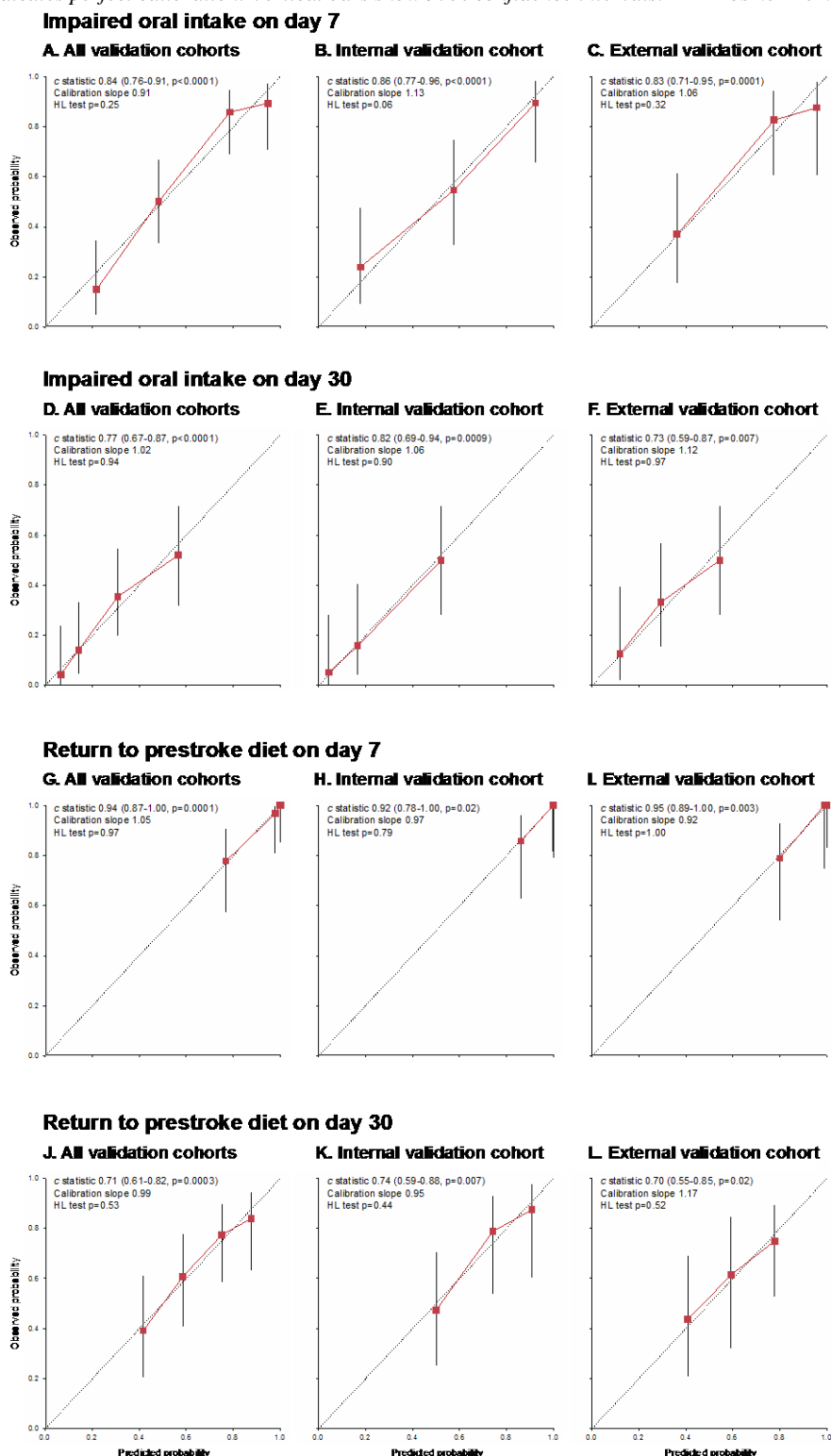
7 Performance of a model previously proposed in literature

We determined discrimination and calibration of a model (PEG score) that was previously proposed in literature for the prediction of PEG placement (Dubin *et al.*, 2013). This model did not discriminate well (**Supplementary Figure II**, *c* statistics ranging from 0.54 - 0.58, p ≥ 0.31) between stroke survivors with and without impaired oral intake on day 7 (indication for NGT feeding) and day 30 (indication for PEG feeding). The results were comparably poor in both internal and external validation cohorts. Calibration slopes ranging from -0.01 to 0.65 suggest poor agreement between observed and predicted outcomes. The Hosmer-Lemeshow test detected significant miscalibration for predicting impaired oral intake on day 30 in the external validation cohort. The calibration plots (**Supplementary Figure II**) also suggest that the prediction estimates from the PEG score do not cover the whole spectrum of low-risk to high-risk cases but rather tend to converge around a similar prediction estimate, which is also indicative of poor discrimination.

To conclude, this previously reported model (PEG score) was not appropriate to guide the need for enteral tube feeding in ischemic stroke survivors. The Predictive Swallowing Score (PRESS) proposed in the current study performed markedly better than the PEG Score in all prognostic aspects (see Results in main manuscript).

Supplementary Figure II: *Calibration plots for a previously proposed model of PEG placement (PEG score)*
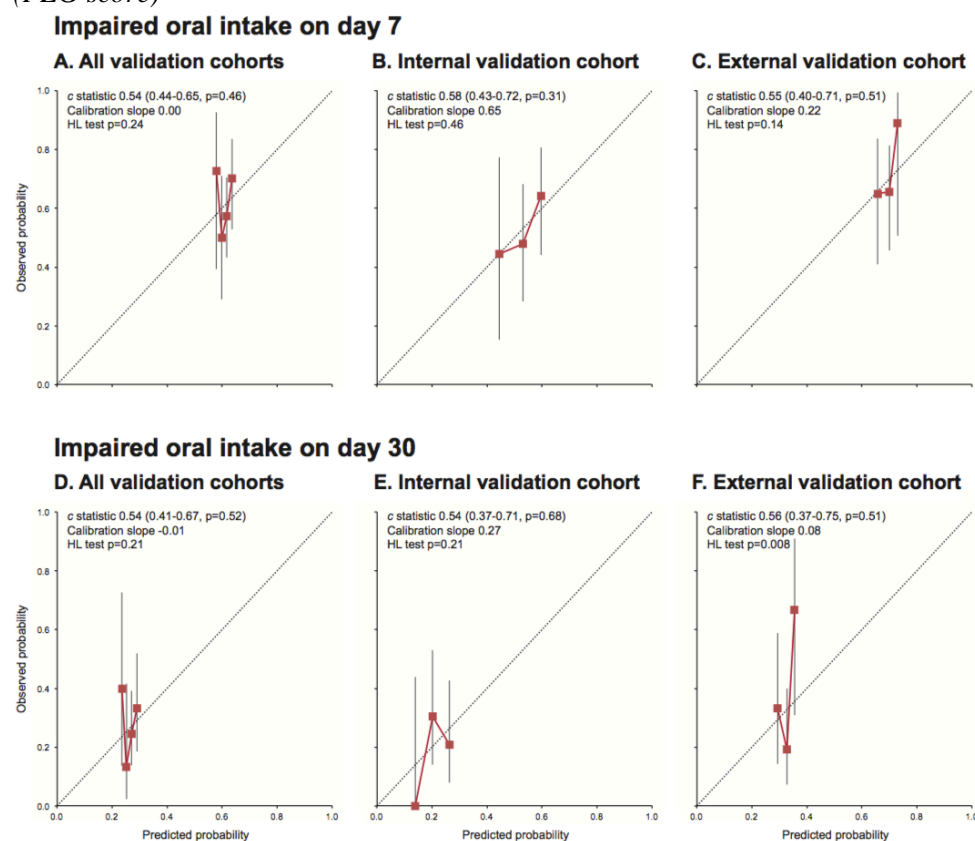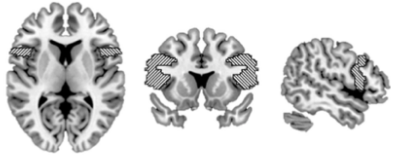

Calibration plots for predicting impaired oral intake on day 7 and day 30 using a previously proposed model for PEG placement (PEG score). Separate plots are displayed for the internal and external validation cohorts. Diagonal line indicates perfect calibration. Vertical bars show 95% confidence intervals. HL=Hosmer-Lemeshow.

Reference for previously proposed model:

Dubin PH, Boehme AK, Siegler JE, et al. New model for predicting surgical feeding tube placement in patients with an acute stroke event. Stroke 2013; 44: 3232–4

8 Example PRESS calculation

Age
- ☐ **0 points**   Age < 70 years
- ☑ **1 point**   Age ≥ 70 years

NIH Stroke Scale at admission
- ☐ **0 points**   NIHSS ≤ 5 points
- ☑ **1 point**   NIHSS = 6 - 13 points
- ☐ **2 points**   NIHSS ≥ 14 points

Stroke location
- ☐ **0 points**   No lesion of the frontal operculum
- ☑ **1 point**   Lesion of the frontal operculum

Initial risk of aspiration
- ☐ **0 points**   Any 2 = 0-3 points
- ☑ **1 point**   Any 2 = 4-5 points
- ☐ **2 points**   Any 2 = 6 points

Any 2 (Daniels et al. 1997)
- ☐ Dysphonia
- ☐ Dysarthria
- ☑ Abnormal gag reflex
- ☑ Abnormal volitional cough
- ☑ Cough after swallow
- ☑ Voice change after swallow

Initial impairment of oral intake
- ☐ **0 points**   FOIS ≥ 4
- ☑ **2 points**   FOIS = 2-3
- ☐ **4 points**   FOIS = 1

FOIS (Functional Oral Intake Scale, Crary et al. 2005)
- ☐ Level 1: Nothing by mouth.
- ☑ Level 2: Tube dependent with minimal attempts of food or liquid.
- ☐ Level 3: Tube dependent with consistent oral intake of food or liquid.
- ☐ Level 4: Total oral diet of a single consistency.
- ☐ Level 5: Total oral diet with multiple consistencies, but requiring special preparation or compensations.
- ☐ Level 6: Total oral diet with multiple consistencies without special preparation, but with specific food limitations.
- ☐ Level 7: Total oral diet with no restrictions.
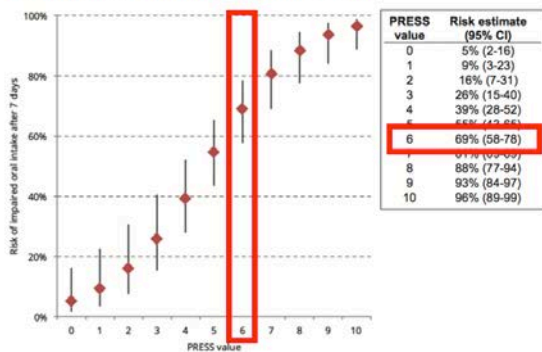
6   **SUM**
(0-10 points)

As an example, a 75-year-old stroke survivor with NIHSS of 10 points, lesion of the frontal operculum, moderate risk of aspiration (Any 2 scale = 4 points), and minimal attempts of food or liquid (FOIS Level 2) has a PRESS of 6 points.
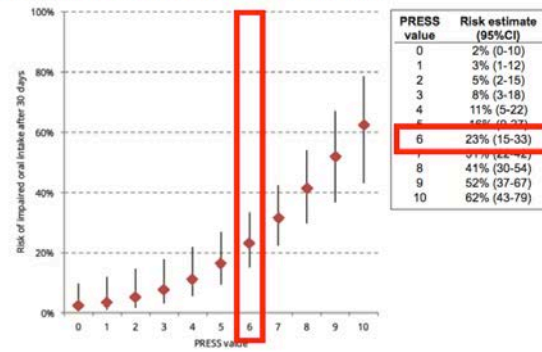
Prediction estimates (see figure below) indicate a 69% (58-78) risk of impaired oral intake on day 7 (indication for NGT feeding), compared to a 23% (15-33) risk on day 30 (indication for PEG feeding).

In this case, the clinician might consider early enteral tube feeding with NGT, whereas it seems unlikely that this individual would benefit from PEG feeding at this early stage.

A. Impaired oral intake after 7 days

PRESS value	Risk estimate (95% CI)
0	5% (2-16)
1	9% (3-23)
2	16% (7-31)
3	26% (15-40)
4	39% (28-52)
5	55% (43-65)
6	69% (58-78)
7	81% (69-89)
8	88% (77-94)
9	93% (84-97)
10	96% (89-99)

B. Impaired oral intake after 30 days

PRESS value	Risk estimate (95%CI)
0	2% (0-10)
1	3% (1-12)
2	5% (2-15)
3	8% (3-18)
4	11% (5-22)
5	16% (9-27)
6	23% (15-33)
7	31% (22-42)
8	41% (30-54)
9	52% (37-67)
10	62% (43-79)

9 Classification parameters for PRESS cut-offs

Supplementary Table IV: *Classification parameters to predict recovery of functional oral intake for different PRESS value cut-offs.*

PRESS cut-off	Impaired oral intake day 7 (indication for NGT feeding)					Impaired oral intake day 30 (indication for PEG feeding)			
	Sensitivity	Specificity	PPV	NPV		Sensitivity	Specificity	PPV	NPV
≥ 1	100%	2%	62%	100%		100%	1%	27%	100%
≥ 2	100%	7%	63%	100%		100%	4%	28%	100%
≥ 3	100%	20%	67%	100%		100%	9%	29%	100%
≥ 4	95%	50%	75%	85%		97%	28%	33%	96%
≥ 5	84%	61%	78%	70%		90%	41%	36%	91%
≥ 6	74%	83%	87%	67%		83%	59%	43%	90%
≥ 7	61%	89%	90%	59%		72%	69%	47%	87%
≥ 8	44%	91%	89%	49%		55%	79%	50%	83%
≥ 9	34%	93%	89%	47%		45%	85%	52%	80%
≥ 10	15%	98%	92%	42%		24%	96%	70%	77%

NGT = nasogastric tube, PEG = percutaneous endoscopic gastrostomy, PPV = positive predictive value, NPV = negative predictive value

Supplementary Table V: *Classification parameters to predict failed return to prestroke diet for different PRESS cut-offs.*

PRESS cut-off	No return to prestroke diet day 7					No return to prestroke diet day 30			
	Sensitivity	Specificity	PPV	NPV		Sensitivity	Specificity	PPV	NPV
≥ 1	99%	0%	94%	0%		100%	3%	67%	100%
≥ 2	99%	29%	96%	67%		100%	8%	68%	100%
≥ 3	96%	71%	98%	56%		100%	19%	71%	100%
≥ 4	81%	86%	99%	22%		87%	39%	74%	61%
≥ 5	71%	100%	100%	18%		77%	53%	76%	54%
≥ 6	56%	100%	100%	12%		63%	69%	80%	49%
≥ 7	44%	100%	100%	10%		51%	75%	80%	44%
≥ 8	31%	100%	100%	8%		37%	83%	81%	40%
≥ 9	25%	100%	100%	8%		30%	89%	84%	39%
≥ 10	11%	100%	100%	6%		13%	97%	90%	36%

NGT = nasogastric tube, PEG = percutaneous endoscopic gastrostomy, PPV = positive predictive value, NPV = negative predictive value

10 Plausibility of factors in cluded in the PRESS model

Age is a relevant predictor of unfavourable outcome after stroke (Saposnik *et al.* 2011) as older individuals are more likely to have reduced neuronal plasticity (Li *et al.* 2010), which might slow swallowing rehabilitation. A more severe neurological deficit leading to higher NIHSS, e.g. sensory disturbances, visual field defects, neglect, or reduced level of consciousness, might indirectly impair the multisensory process of swallowing and interfere with participation in swallowing training, thus, slowing recovery. Specific stroke location involving the frontal operculum might lead to impaired recovery through the disruption of perilesional neuronal plasticity (Galovic *et al.* 2013) or via acting as a premotor area for swallowing (Galovic *et al.* 2016). Lastly, the role of initial impairment of oral intake and initial risk of aspiration highlights the importance of an early assessment of the initial severity and type of swallowing impairment.

References:

Galovic M, Leisi N, Müller M, *et al.* Lesion location predicts transient and extended risk of aspiration after supratentorial ischemic stroke. *Stroke* 2013; **44**: 2760-7.

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