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Association between Hunt and Hess grading scale and the modified Rankin Scale among patients with non-traumatic subarachnoid hemorrhage

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ABSTRACT

Association between Hunt and Hess Grade and the Modified Rankin Scale among Patients with Non-Traumatic Subarachnoid Hemorrhage

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- **Background:** Hunt and Hess (HH) grading scale is the most utilized scale to describe the clinical status of patients admitted with non-traumatic subarachnoid hemorrhage (SAH). Upon discharge, the modified Rankin Scale (mRS) is used to evaluate patient's outcome. The relationship between HH on admission and mRS upon discharge has not been evaluated before. In this study we aimed to evaluate this relationship among patients admitted to the Neuro-Intensive Care Unit (NICU).
- **Methods:** This retrospective analysis was based on data from patients with non-traumatic SAH admitted to Emory University Hospital NICU during the period 2006-2016. The data included patients' demographics, smoking status, associated diseases related to SAH, year of admission, admission's HH grade and discharge's mRS. Univariate and multivariate binary logistic regression analyses were performed to obtain crude and adjusted odds ratios. Rates of HH grade on admission and mRS upon discharge over time were also determined to describe trends in medical care at this institution.
- **Results:** 2672 patients were enrolled in the study**.** The median age was 54 years (range: 12-101). 66% of patients were female, 42% were white and 30% were black. 26% of the patients were smokers, 54% hypertensive and 12% were diabetic. 8% had a history of coronary artery disease or myocardial infarction (CAD/MI) and 14% had a history of hyperlipidemia. In the multivariable analysis, the odds ratio for bad outcome mRS (3-6) was 5.7 *(95% C.I: 4.6-7.0)* and 66.0 (*95% CI: 44.0-99.1*) for the intermediate-grade (III) and high-grade (IV and V) HH groups respectively, when compared to the low-grade (I and II) HH group. Age, hypertension and diabetes were found to be negatively associated with the mRS outcome, while hyperlipidemia was found to be positively associated. Gender, race, smoking status and history of CAD/MI were not related to the mRS outcome. A positive trend for a better mRS outcome was observed across years. There was no evidence that the significant trend was related to HH grade on admission, suggesting better medical and/or surgical management for this

patient population across years (p=0.18 for interaction between HH grade and year).

- **Conclusion:** HH grading scale on admission is associated with the mRS outcome upon discharge for patients with non-traumatic SAH. Models predicting the probability of a good mRS outcome could be created and validated based on the HH grade on admission, age, hypertension, diabetes and hyperlipidemia status.

Key words: Non-traumatic Subarachnoid Hemorrhage; Hunt and Hess grading scale; modified Rankin Scale

Abbreviations:
SAH: Subarachnoid hemorrhage; HH: Hunt and Hess (scale); mRS: Modified Rankin Scale; NICU: Neuro-Intensive Care Unit; CAD/MI: Coronary Artery Disease/ Myocardial Infarction.

ACKNOWLEDGEMENT

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BACKGROUND

The Hunt and Hess (HH) grading scale was developed in 1968 in order to evaluate the appropriate timing and potential risk for surgery for patients with non-traumatic aneurysmal subarachnoid hemorrhage (SAH)[1, 2]. The scale was mainly developed based on the three most important symptoms and signs of subarachnoid hemorrhage which are: (1) evidence and severity of meningeal irritation such as headache and nuchal rigidity, (2) the severity of neurological deficit, and (3) the level of arousal (see figure 1). Additionally, presence of a serious associated systemic disease such as hypertension, diabetes or chronic obstructive pulmonary disease (COPD), or presence of severe vasospasm on angiography is also applied to the scale by placing the patient in the next less favorable category [1]. The scale is widely known to the neuroscience community, and the original article by Hunt and Hess is one of the most commonly cited articles in the neurosurgical literature [3]. Many studies have used the Hunt and Hess scale to assess for the outcome of patients with subarachnoid hemorrhage using different outcome measures including Glasgow Outcome Scale (GOS) [4-6] and other measures of outcome [7].

The Rankin scale was developed by John Rankin of Scotland in 1957 to assess motor disability for stroke patients [8]. This scale was later modified by Warlow et al in the late 1980s to become the currently widely used "modified Rankin Scale" (figure 2) [9, 10]. The modified Rankin Scale (mRS) subsequently has been shown to have very strong validity and reliability as a measure of outcome for stroke patients [11].

Although the managment may vary on case by case basis, some authors claim that the discharg outcome for patients is highly dependant on their presenting Hunt and Hess admission's grade [13] .To date, only a few studies have been done to evaluate the direct or indirect relationship between Hunt and Hess grading scale and the clinical outcome measured by mRS [12, 13]. In 2014, Suchdev et al retrospectively studied the association between the two scales [13]. Although a strongly positive association was found (HH odds ratio 0.384 [0.258-0.574]), the study involved only 141 subjects from two different institutes. In this study, we investigate the association between Hunt and Hess grading scale on admission and the corresponding modified Rankin scale upon discharge for patients with non-traumatic spontaneous subarachnoid hemorrhage. We also wish to evaluate the trend of Hunt and Hess grading scale and the corresponding modified Rankin scale across years to describe the progress of medical care across years at our institution.

Figure 1: Hunt and Hess grading scale[1] :

I	Asymptomatic, or mild headache and slight nuchal rigidity
II	Cranial nerve palsy, moderate to severe headache, nuchal rigidity
III	Mild focal deficit, lethargy, or confusion
IV	Stupor, moderate to severe hemiparesis, early decerebrate rigidity

V	Deep coma, decerebrate rigidity, moribund appearance

Figure 2: The original and modified Rankin Scale [11] :

Grade	Original RS	mRS
0	NA	No symptoms at all
1	No significant disability: able to carry out all usual duties	No significant disability: despite symptoms, able to carry out all usual duties and activities
2	Slight disability: unable to carry out some of previous activities but able to look after own affairs without assistance	Slight disability: unable to perform all previous activities but able to look after own affairs without assistance
3	Moderate disability: requiring some help but able to walk without assistance	Moderate disability: requiring some help but able to walk without assistance
4	Moderately severe disability: unable	Moderately severe disability: unable

Grade	Original RS	mRS
	to walk without assistance, and unable to attend to own bodily needs without assistance	to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability: bedridden, incontinent and requiring constant nursing care and attention	Severe disability: bedridden, incontinent and requiring constant nursing care and attention
6	Not applicable	Death

METHODS

Data Source:

Data registry in MS Excel file for all patients admitted to the neuro ICU at Emory University Hospital during the period 2002-2016 with the diagnosis of spontaneous non-traumatic subarachnoid hemorrhage (SAH) . Patients information was imported to Excel from the electronic medical records system (Power Chart) used at Emory University Hospital. Patient demographic data were collected including: age, gender, race, smoking status, presence of chronic diseases related to the outcome of subarachnoid hemorrhage including: hypertension, diabetes, history of coronary arterial disease or myocardial infarction and hyperlipidemia. Emory University Institutional Review Board (IRB) approval was obtained for the study.

Study Population:

Patients who with non-traumatic spontaneous subarachnoid hemorrhage admitted to the neurological ICU at Emory University Hospital for the period 2006 to 2016. Patients admitted to the ICU before 2006 were excluded since the primary outcome variable (modified Rankin Scale score) was not reported prior to this year. Patients with repeated admission to the neuro ICU due to rebleeding or other causes were excluded from the study due to the possibility of the pre-existing abnormal mRS as a result of prior bleeding.

Dependent Variable (modified Rankin Scale, mRS):

The primary outcome variable in the study was the modified Rankin Scale (grade 0-6) [11] which was dichotomized to good outcome (defined by mRS of 0-2) or bad outcome (mRS 3-6) [11, 12]

Independent Variable (HH scale) :

The primary independent variable was Hunt and Hess grade on admission which was reported from 1-5 [1] . To facilitate the analysis, the Hunt and Hess scale was later recategorized as low-grade (I+II), intermediate-grade (III), and high-grade (IV+V) [1, 2].

Co-variables:

We examined the following covariables in our analysis: patient's age (which was treated as numeric variable and also categorized into (< 40, 40-59, 60-79 and 80 years or more). gender status (male, female), race (white, black and others/unidentified), smoking status (smoker, non-smoker), history of hypertension (yes, no), history of diabetes milletus (yes, no), history of chronic artery disease or myocardial infarction (yes, no), history of hyperlipidemia (yes, no), and year of admission (2006-2016).

Statistical analysis:

We examined the crude and adjusted association between the Hunt and Hess grade on admission and the modified Rankin Scale upon discharge using binary logistic regression analysis. Univariable and multivariable analysis was done including all of the covariates mentioned above. Odds ratios were reported with 95% confidence intervals.

A final regression model was then obtained using stepwise regression. The significance of the interaction between the Hunt and Hess grade and year of admission was assessed to determine whether the pattern of change in the modified Rankin Scale over time depended on the Hunt and Hess grade during admission. SAS$^®$ version 9.4 (SAS Institute Inc., Cary, NC) was used for the analysis.

RESULTS

Two thousand, six hundred and seventy two patients were included in the study. The median age was 54 years (12-101). 1753 patients were female (66%). 42% of the patients were white and 30% were black. The rest were either other race or unidentified. 26% of

the patients were smokers, 54% hypertensive and 12% were diabetic. 8% had a history of coronary artery disease or myocardial infarction (CAD/MI) and 14% had a history of hyperlipidemia. Table 1 shows the demographic distribution for the patient population overall and for each HH group. The good outcome mRS was observed in 50% of patients. However, when the patients were grouped according to their Hunt and Hess grade upon admission the good mRS outcome was observed in 76%, 39% and 6% of the low, intermediate and high Hunt and Hess grades, respectively (table 2).

Significant association was observed between the HH grade on admission and the mRS upon discharge. In the univariate analysis, the odds ratio for having bad mRS when the intermediate HH group was compared to the low HH group was 5.10 *(95% C.I.: 4.22, 6.16).* When the high HH group was compared to the low HH group, the odds ratio increased dramatically to 53.09 *(95% C.I.: 36.13, 78.01).* Table 3 shows adjusted odds ratios in the multivariable analysis. Among the other variables, age, hypertension, diabetes were negatively associated with the mRS outcome, while the year of admission was positively associated with the outcome in both univariable and multivariable analyses. Sex, race and smoking status were not significantly associated with the outcome in either univariable or multivariable analysis. History of coronary arterial disease or myocardial infarction was significantly associated with the outcome in the univariable analysis but not in the multivariable analysis. On the other hand, hyperlipidemia was positively associated with the outcome in the multivariable analysis but not in the univariable analysis. Following stepwise regression technique, a final model was obtained with mRS as the response variableand Hunt and Hess grade, age,

hypertension, diabetes, hyperlipidemia and the year of admission as the explanatory variables (table 4).

The trend of admission based on the Hunt and Hess scale and discharge based on the mRS was also assessed across years (figures 3 and 4). The trend for a better mRS outcome over time was significant in both univariable and multivariable analysis (crude OR for bad outcome mRS: 0.96 (*95% C.I: 0.94, 0.99)* and *adjusted OR:* 0.90 *(95% C.I: 0.87, 0.93*). The interaction between the year of admission and the HH grade was not significant (p=0.18), suggesting that the trend of a better mRS outcome over time was not dependent on the HH grade on admission. That functional outcome status upon discharge has significantly changed over time suggests an improvement in the medical or surgical care for this patient population.

DISCUSSION

Hunt and Hess grading scale is the most frequently and widely utilized scale to predict surgical outcome for patients with aneurysmal subarachnoid hemorrhage [1, 2]. To our knowledge, only a single study has investigated the association between the Hunt and Hess scale and the patient outcome as measured by the mRS. However, that study used a relatively small sample size (n=?). Moreover, it was collected from two separate institutions which could have different protocols of management [13]. We describe a large patient-volume single-institute retrospective study to investigate this association. Our findings suggest a strong positive association between the HH grade on admission and the mRS upon discharge. The worse HH grade on admission was strongly associated with the worse mRS upon discharge, controlling for other factors such as age, gender, race, smoking status and associated diseases: hypertension, diabetes, hyperlipidemia and history of CAD/MI. Additionally, we also found that increased age, hypertension and diabetes were associated with worse mRS outcome. Although the later finding was also described in several articles in the literature, the outcome measurements used in those studies were different from the mRS [14-16]. Our finding of the positive association between hyperlipidemia and good outcome mRS has also been suggested in some articles [17, 18]. A plausible cause for this finding is that patients with hyperlipidemia were already on statin therapy which may confer a protective effect against subsequent vasospasm and overall mortality [19]. The observed trend of the improved mRS outcome across years despite no improvement in the HH grade on admission suggests a longitudinal improvement in the overall medical and or surgical care services provided

for our patients through the period of the study. However, further categorization for etiology of the subarachnoid hemorrhage and the intervention applied is needed to further validate this suggestion. Finally, we obtained a regression model that identified the explanatory variables that were most significantly associated with the mRS outcome.

This study also has some limitations. We have included all patients with non-traumatic SAH regardless of their etiology. Although the majority of the cases were aneurysmal in etiology, other causes of non-traumatic SAH should also be considered, and perhaps controlled for, in order to achieve a more precise measurement of association. Additionally, subsequent intervention for patients with aneurysmal SAH (surgical clipping versus coiling versus no intervention) was not considered in the analysis; it is possible that the type of intervention significantly modifies the association between HH and the outcome [20]. We are planning for a a more comprehensive study that includes both the etiology and the type of the intervention for a better assessment of the association and perhaps prediction of the mRS outcome based on the admission's HH grade and all associated covariates.

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Table 1: Demographic characteristics of patients with non-traumatic SAH admitted to the NICU during 2006-2016 (N= 2672)

Characteristics	All	HH (I + II)	HH(III)	HH (IV+V)
Age (median and range) years	54 (12 -101)	52 (12-98)	54 (15-101)	56 (14-90)
Gender (N and %)				
• **Females**	1753 (66%)	810 (64%)	582 (68%)	361 (66%)
Race (N and %)				
• **White**	1128 (42%)	567 (45%)	337 (39%)	224 (41%)
• **Black**	808 (30%)	373 (29%)	285 (33%)	150 (28%)
Smoker (N and %)				
• **Yes**	685 (26%)	336 (27%)	229 (27%)	120 (23%)
Hypertension (N and %)				
• **Yes**	1427 (54%)	584 (46%)	520 (61%)	323 (62%)
Diabetes (N and %)				
• **Yes**	316(12%)	142 (11%)	97 (11%)	77 (15%)
History of CAD/ MI (N and %)				
• **Yes**	217(8%)	85 (7%)	74 (9%)	58 (11%)
Hyperlipidemia (N and %)				
• **Yes**	379 (14%)	194 (15%)	112 (13%)	73 (14%)
Total (N and %)	**2672 (100%)**	**1269 (48%)**	**858 (32%)**	**545 (20%)**

HH= Hunt and Hess grade, CAD/MI=coronary artery disease/ myocardial infarction

Table 2: Good mRS (0-2) outcome upon discharge stratified by HH grade for patients with non-traumatic SAH (N= 2672):

	All	HH (I + II)	HH(III)	HH (IV+V)
Good outcome (0-2) (N and %)	1329 (50%)	967 (76%)	331 (39%)	31 (6%)

HH= Hunt and Hess grade

Table 3 : Univariable and multivariable analyses for bad mRS outcome, (N= 2672):

Characteristic	Bad mRS (3-6) N (%)	Univariable Analysis		Multivariable Analysis	
		cOR	(95% C.I.)	aOR	(95% C.I.)
HH Group:					
• **HH (III) vs (I+II)**	527 (61%)	5.098	(4.222, 6.156)	5.656	(4.600, 6.955)
• **HH (IV+V) vs (I+II)**	514 (94%)	53.091	(36.132, 78.009)	65.982	(43.943, 99.074)
• **HH (I+II)**	302 (24%)	-	-	-	-
Age : Overall age	-	1.038	(1.032, 1.045)	1.044	(1.036, 1.052)
• **(40-59) vs (<40) years**	591(44%)	1.367	(1.089,1.715)	1.091	(0.819, 1.452)
• **(60-79) vs (<40) years**	500(64%)	3.089	(2.412, 3.956)	2.914	(2.105, 4.033)
• **(≥80) vs (<40) years**	101(80%)	6.792	(4.223, 10.923)	8.701	(4.924, 15.375)
• **(<40) years**	151 (36%)	-	-	-	-
Gender :					
• **Female vs Male**	886 (51%)	1.033	(0.881, 1.212)	0.878	(0.715, 1.077)
• **Male**	457 (50%)	-	-	-	-
Race:					
• **(Black vs White)**	405 (50%)	0.960	(0.801, 1.150)	1.023	(0.806, 1.297)
• **(Other vs White)**	361(49%)	0.919	(0.763, 1.107)	0.821	(0.646, 1.043)
• **(White)**	577(51%)	-	-	-	-
Smoking	329 (48%)	0.922	(0.775, 1.098)	1.146	(0.919, 1.429)
Hypertension	813 (57%)	1.929	(1.651, 2.254)	1.234	(1.001, 1.521)
Diabetes	191(60%)	1.653	(1.301, 2.101)	1.386	(1.017, 1.888)
History of CAD/MI	136 (63%)	1.794	(1.347, 2.389)	0.895	(0.612, 1.308)
Hyperlipidemia	191(50%)	1.041	(0.837, 1.294)	0.742	(0.553, 0.994)
Year of the event	-	0.964	(0.939, 0.990)	0.896	(0.865, 0.927)

mRS=modified Rankin Scale cOR=crude odds ratio; aOR=adjusted odds ratio; CI=confidence interval; HH=Hunt and Hess grade

Table 4: A prediction model for the mRS outcome   based on the final multivariate analysis and the backward elimination process.

| | *Multivariate Analysis* | | |
	aOR	*(95% C.I.)*	*P value*
HH (III) vs (I+II)	5.573	*(4.538, 6.844)*	0.0043
HH (IV+V) vs (I+II)	63.455	*(42.381, 95.009)*	<.0001
Age	1.042	*(1.035, 1.050)*	<.0001
Hypertension	1.251	*(1.020, 1.535)*	0.0317
Diabetes	1.372	*(1.012, 1.861)*	0.0420
Hyperlipidemia	0.737	*(0.554, 0.981)*	0.0366
Year of the event	0.897	*(0.867, 0.929)*	<.0001

aOR= adjusted Odds Ratio; CI= Confidence Interval; HH= Hunt and Hess grade.
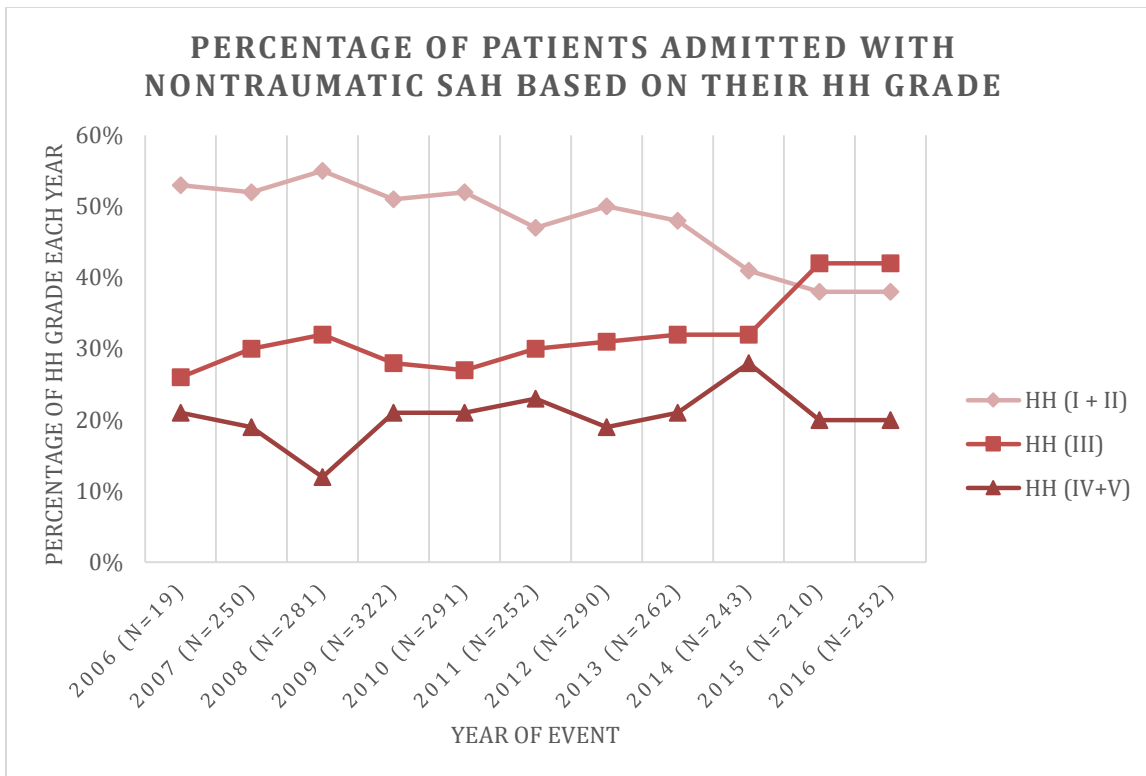
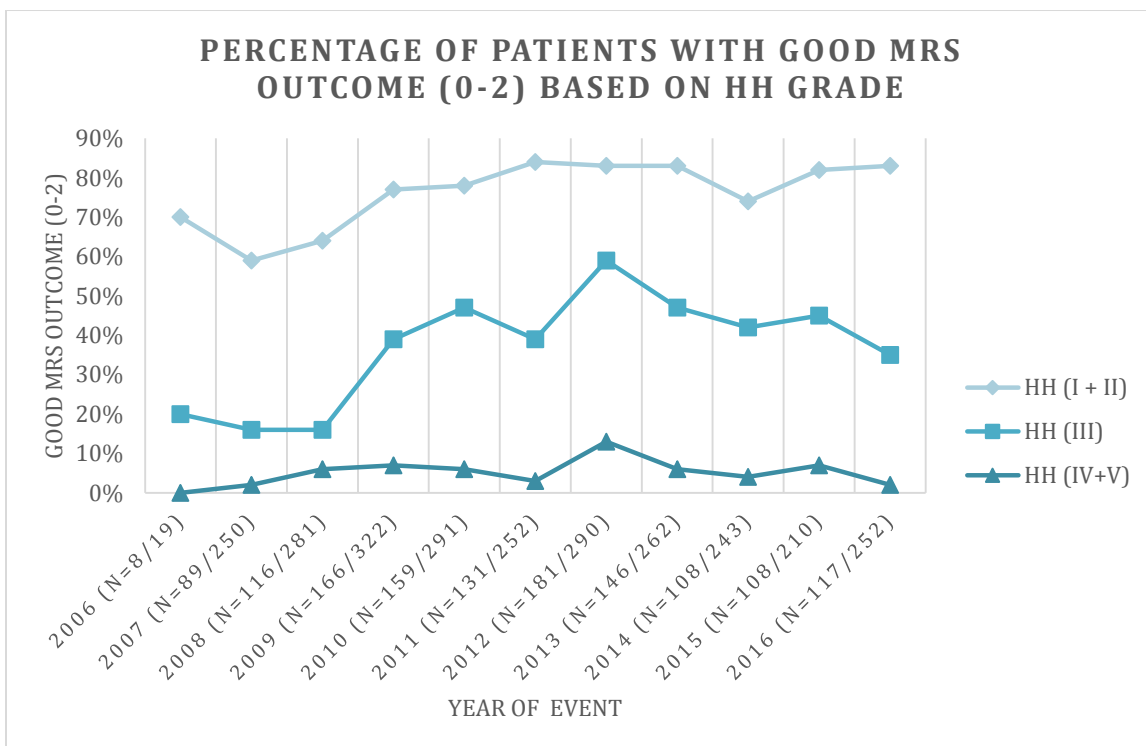**Figure 3: Trend of HH grade during admission across years**
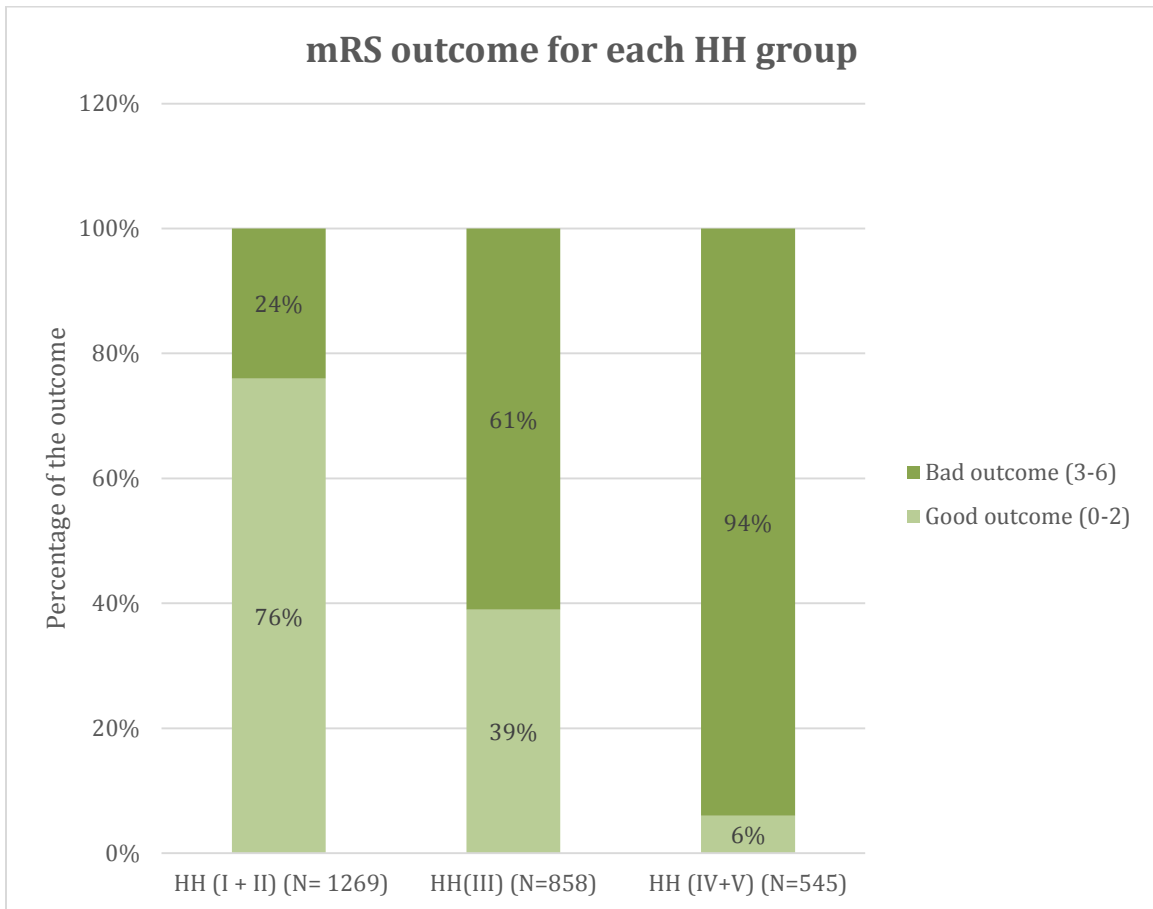

Figure 4: Trend of good mRS (0-2) outcome across years

Figure 5: mRS outcome according to HH group