FALL PREDICTORS IN MULTIPLE SCLEROSIS: AN EXPLORATORY ANALYSIS

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Background

- Falls and its consequences form a major health concern in persons with Multiple Sclerosis (PwMS).
- Due to its multifactorial nature, it is vital to investigate the prime determinants that distinguish 'high-risk' fallers from those with a lesser risk.

Objectives

- To identify the significant contributors with respect to demographics, strength, balance, functional mobility, spasticity, self-report measures and cognition that predict falls in PwMS.
- To compare the resulting significant predictors and identify cut-offs for their predictive accuracy of falls in PwMS.

Methods

- Pilot, cross-sectional design with retrospective fall history.
- Sample of convenience (n=55).
- Criteria for inclusion: Clinically definite MS.
- Criteria for exclusion: Recent or current acute exacerbation.

Table 1: Sample descriptive [Mean (Range)]

Variable	Total sample (n=55)	Non-fallers (n=17)	Fallen at least once (n=34)	Recurrent fallers (n=25)	Others (0 or 1 fall, n=26)
Age (yrs)	56.2 (23-81)	57.5 (31-81)	56.7 (23-77)	56.6 (23-77)	57.3 (31-81)
Gender (F/M)	38/17	12/5	23/11	15/10	20/6
Height (cm)	168 (147-191)	169 (153-191)	167 (147-185)	168 (147-185)	167 (152-191)
Weight (kg)	78 (49-135)	74 (50-106)	77 (49-135)	77 (51-100)	76 (49-135)
EDSS	5.3 (3-8)	4.6 (3-8)	5.6 (3.5-7.5)	5.7 (3.5-7.5)	4.9 (3-8)
Time since diagnosis	14.3 (1-41)	11.6 (3-34)	16.9 (1-41)	15.5 (1-39)	14.8 (3-41)
ABC (%)	56 (0-97.8)	66.9 (6-94.7)	50.9 (4.7-97.8)	50.7 (4.7-97.8)	61.5 (5-94.7)
ASH-ave	0.55 (0-3)	0.35 (0-3)	0.65 (0-3)	0.76 (0-3)	0.35 (0-3)
SDMT	42.4 (11-63)	44.7 (32-55)	41.3 (11-63)	39.9 (11-60)	44.8 (21-63)

Instruments and Measures

The outcome (or the dependent) variable

- For multiple linear regression analysis, the number of falls recalled in the past year was used (falls/yr).
- For hierarchical binary logistic analysis, two separate dichotomous variables comparing all falls versus no fall events and recurrent falls (2 or more falls) versus others (0 or 1 fall) were created and utilized.

The predictor (or the independent) variables: Seven covariates based on existing literature were identified.

- **Demographics** included age, gender and EDSS scores.
- **Strength** determined by the average of maximal isometric knee extensor strength for both extremities.
- **Clinical balance** measures included berg balance test and functional reach
- **Functional mobility** measures included timed-up and-go, twenty-five feet walk test, stairs test and six-minute walk distance
- **Spasticity** assessed by the average of modified ashworth scale for both ankle plantarflexors (ASH-ave).
- **Self-report** measures included the multiple sclerosis walking scale, the Activities-specific Balance Confidence scale (ABC), and the modified fatigue impact scale.
- **Cognitive status** measured by paced auditory serial addition test and Symbol Digit Modalities Test (SDMT).

Analysis

The uncertainty regarding the relationship of these variables to falling[1,2] led to no 'a priori' hypothesis.

- **Identification of significant Predictors:** A stepwise multiple regression analysis was performed to find a model that predicts the maximum number of falls in PwMS from the predictor variables.
- **Predictive accuracy:** Then, a hierarchical binary logistic regression model was used to examine the effectiveness of the identified predictors to predict people who fell in the past year. These models either compared all falls versus no reported falls or those with 2 or more (recurrent) falls versus none or 1 fall.
- **Cut-off determination:** The predictors were, thereafter, analyzed using hierarchical logistic regression for improvements in prediction of falls in different cut-off combinations for ABC. The cut-offs which maximized the sensitivity, specificity and the overall model's predictive value were chosen.

SPSS version 20.0 was used for analysis. For regression, missing values were deleted listwise.

Results

Of fifty-five PwMS, 34 (61.8%) reported 156 falls. Of the fallers, 25 (73.5%) reported recurrent falls (>1 fall). In combination, all the predictor variables accounted for 72.3% of the variance in the number of falls.

Identification of predictors

ABC, ASH-ave and SDMT, in the respective order, were found to be the prime predictors, $R^2 = 0.612$, $F(3, 34) = 17.86$, $p<0.0001$, indicating that PwMS who have higher self-reported balance confidence, low levels of spasticity and higher cognitive function tend to have an overall lower number of falls. The assumptions for normality, independence and linearity (except homoscedasticity) were met.

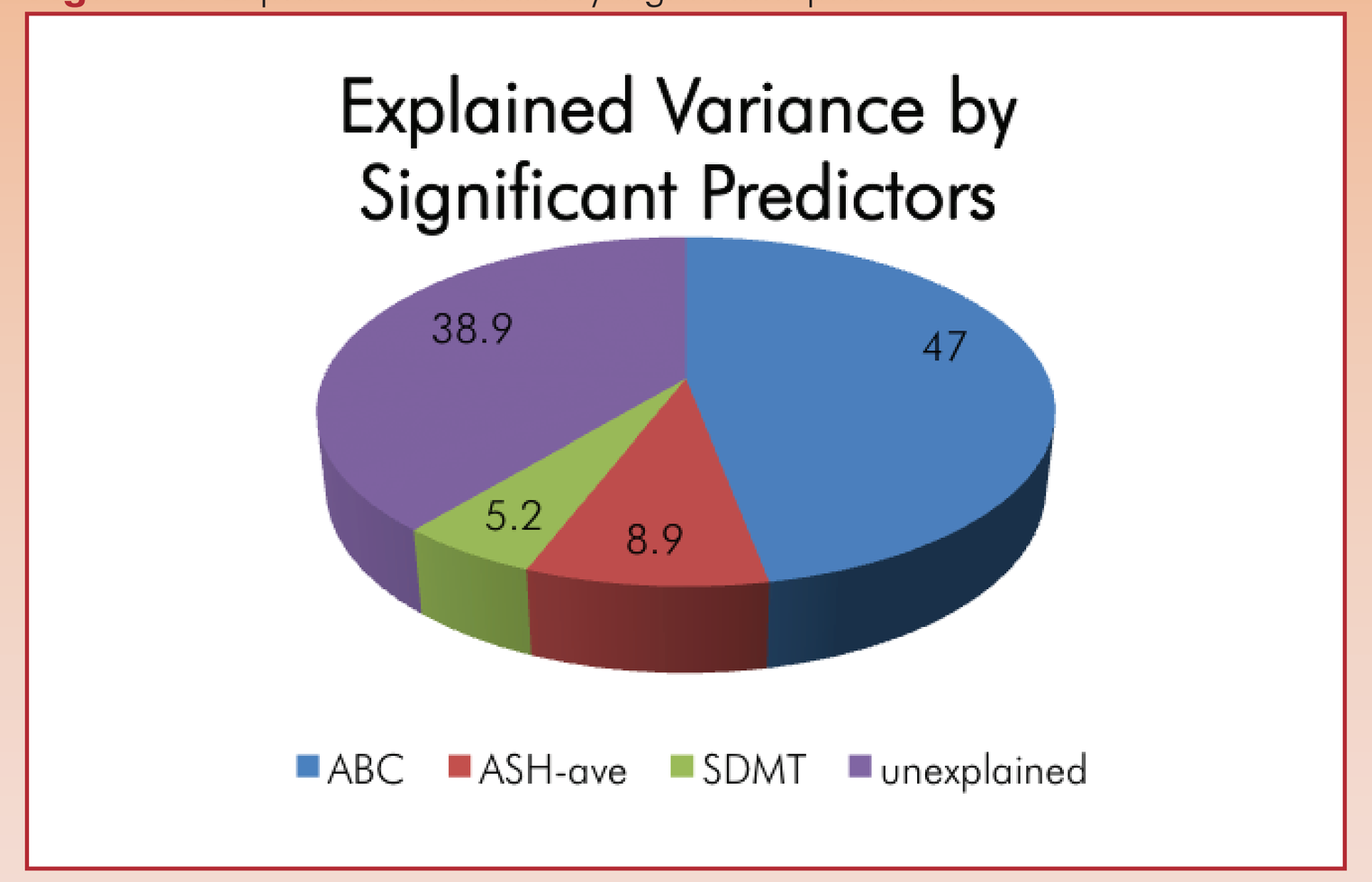
- **The regression equation:** Predicted score (number of falls) = 12.531 – 0.096 (ABC score) + 2.523 (ASH-ave) – 0.091 (SDMT score).v

Table 2: Multiple Linear Regression Model

Model	R	R square	R square change	F change	df1	df2	sig. F change	Durbin Watson
1	0.686	0.470	0.47	31.96	1	36	0.000	1.65
2	0.748	0.560	0.089	7.11	1	35	0.012	
3	0.782	0.612	0.052	4.56	1	34	0.040	

Dependent Variable: Falls/yr
Model 1 Predictors: ABC
Model 2 Predictors: ABC, ASH-ave
Model 3 Predictors: ABC, ASH-ave, SDMT

Figure 1: Explained variance by significant predictors

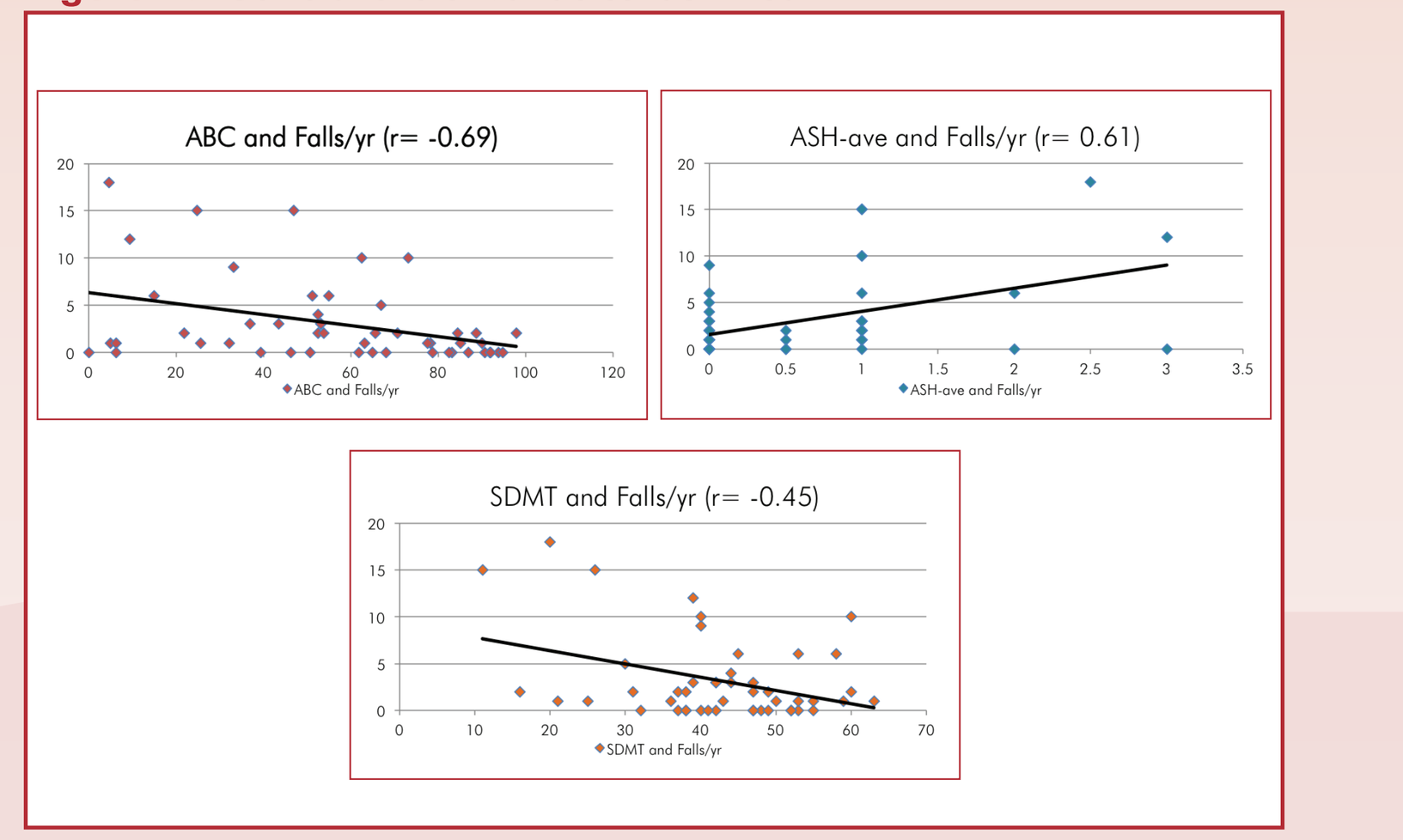


Probability (Predictive accuracy) of model containing ABC, ASH-ave and SDMT

- **Hierarchical Logistic Regression Models:** Fallers vs. Non-fallers

The combined model of all variables was significant and demonstrated that the probability of determining a faller from a non-faller was higher in people with low self-reported balance (ABC), higher spasticity (ASH-ave) and low cognition (SDMT), with ABC found to be the most significant predictor. Interestingly, similar predictive accuracy (78.7% accurate classification of fallers) and explained variance (Nagelkerke R2=0.229) were found in the combined model of SDMT, ASH-ave and ABC, as opposed to a model with ABC as the lone predictor (78.3% accurate and R2=0.264). A cut-off measure of 60 for ABC in the combined model resulted in improvements in specificity & model accuracy. This highlights the ability of a self-report balance measure such as the ABC to accurately distinguish PwMS with 'high-risk' of falls.

Figure 2: Correlations of variables identified



Hierarchical Logistic Regression Models: Recurrent Fallers vs. Others (0 or 1 fall)

- The combined model approached significance (p=0.06) and demonstrated that the probability of determining a recurrent faller from others was higher in people with low cognition (SDMT), higher spasticity (ASH-ave) and low self-reported balance (ABC). Similar predictive accuracy (70.2%) and explained variance (Nagelkerke R2=0.191) were again noted in the combined model as compared to a model with ABC as the lone predictor (71.7% and R2=0.123) indicating the importance of the self-report balance measure. Importantly, a cut-off measure of 60 for ABC in the combined model resulted in a significant model and improvements in sensitivity & model accuracy.

Table 3: HLR models – Fallers vs. Non-fallers (n=47)

Model	Predictors	Coefficients (SE)	Wald's □2 (p)	OR (95%CI)	Overall model □2 (p)	Sensitivity (Sn), Specificity (Sp) (%)	Predictive accuracy (%)	False positive/ False negative rates (%)
1	SDMT	-0.016 (0.03)	0.24 (0.63)	0.98 (0.92-1.05)	8.38 (0.039)	90.6, 53.3	78.7	19.4, 27.3
	ASH-ave	0.243 (0.67)	0.13 (0.71)	1.27 (0.35-4.71)				
	ABC	-0.035 (0.02)	3.95 (0.04)	0.97 (0.93-1.00)				
2	SDMT	-0.011 (0.03)	0.12 (0.73)	0.99 (0.93-1.05)	8.33 (0.04)	87.5, 66.7	80.9	15.1, 28.5
	ASH-ave	0.382 (0.63)	0.37 (0.54)	1.46 (0.43-5.04)				
	ABC (60 cut-off)	-1.64 (0.8)	4.18 (0.04)	0.19 (0.04-0.93)				
3	ABC	-0.045 (0.02)	6.63 (0.01)	0.96 (0.92-0.99)	9.51 (0.002)	87.5, 57.1	78.3	17.6, 33.3

Figure 3: Mean Differences: Fallers vs. Non-Fallers

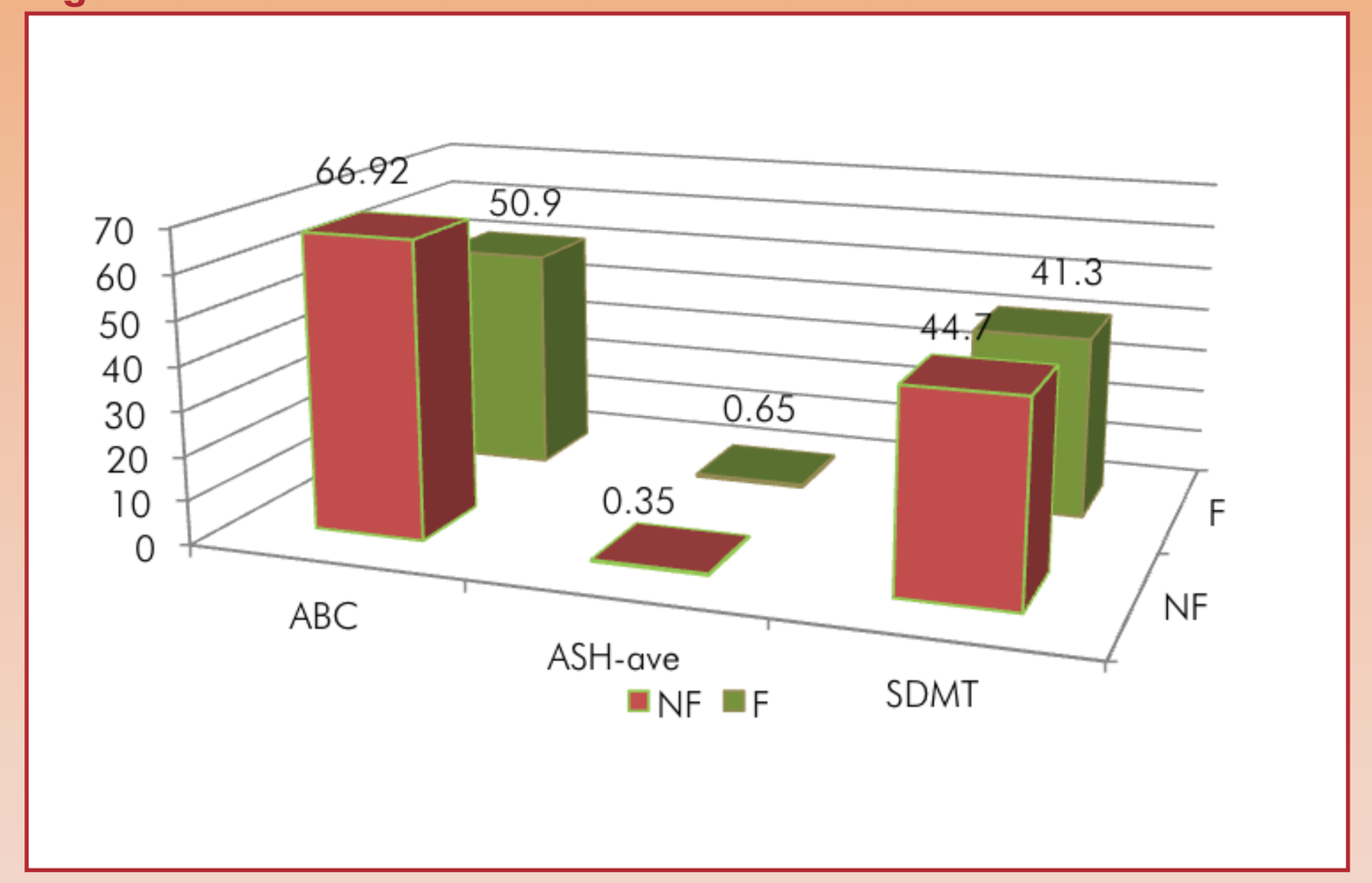


Table 4: HLR models – Recurrent Fallers vs. Others (0 or 1 fall, n=47)

Model	Predictors	Coefficients (SE)	Wald's □2 (p)	OR (95%CI)	Overall model □2 (p)	Sensitivity (Sn), Specificity (Sp) (%)	Predictive accuracy (%)	False positive/ False negative rates (%)
1	SDMT	-0.029 (0.03)	1.02 (0.311)	0.97 (0.92-1.03)	7.25 (0.064)	60.9, 79.2	70.2	26.3, 32.1
	ASH-ave	0.724 (0.55)	1.72 (0.190)	2.06 (0.70-6.08)				
	ABC	-0.012 (0.01)	0.77 (0.38)	0.99 (0.96-1.01)				
2	SDMT	-0.025 (0.03)	0.672 (0.41)	0.98 (0.92-1.03)	10.15 (0.02)	69.6, 75	72.3	27.2, 28
	ASH-ave	0.586 (0.53)	1.21 (0.27)	1.8 (0.63-5.1)				
	ABC (60 cut-off)	-1.307 (0.69)	3.56 (0.06)	0.27 (0.07-1.05)				
3	ABC	-0.024 (0.01)	4.01 (0.045)	0.98 (0.95-0.99)	4.47 (0.035)	69.6, 73.9	71.7	27.3, 29.2

Figure 4: Mean Differences: Recurrent Fallers vs. Others (0 or 1 fall)

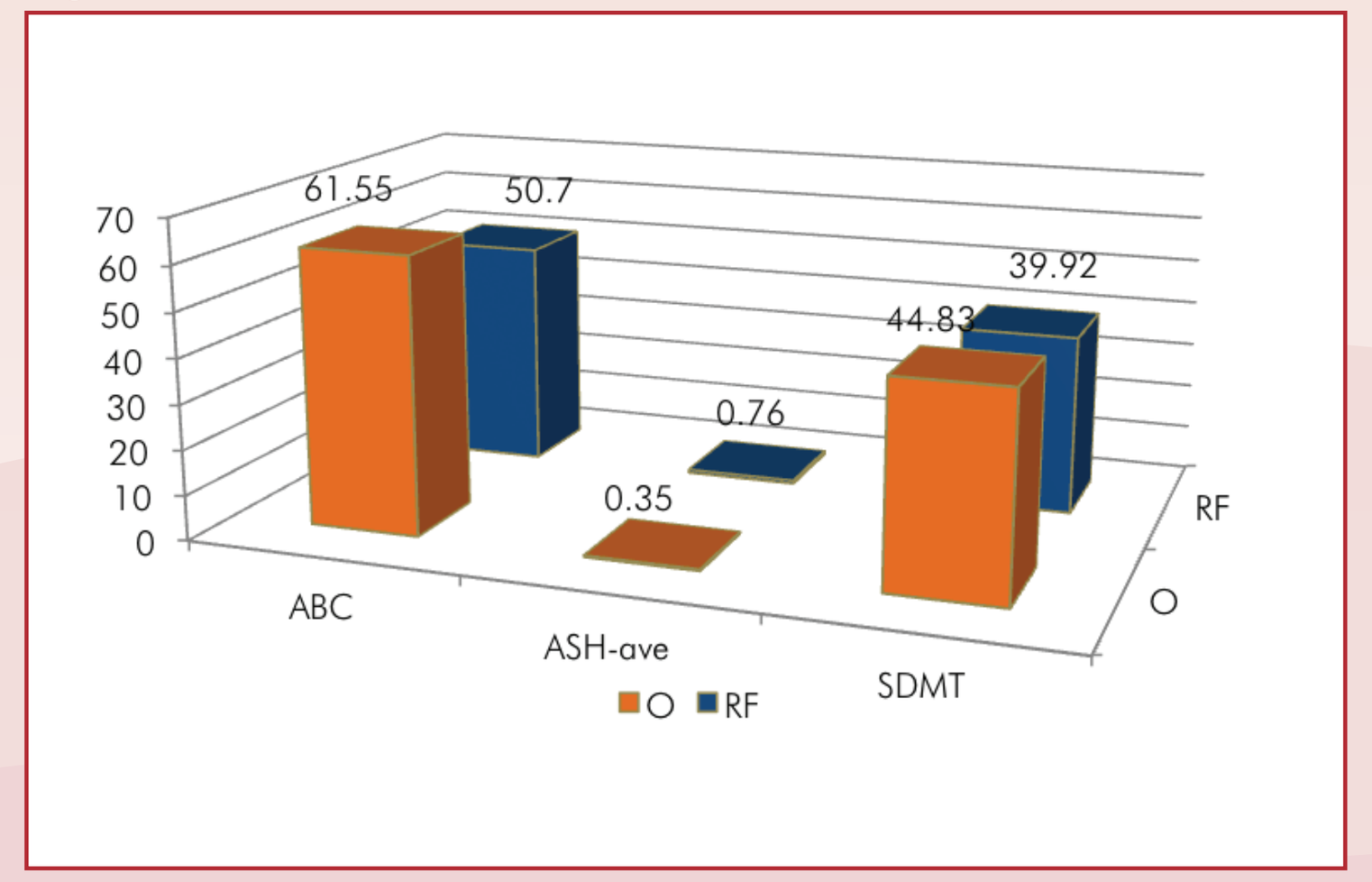


Figure 5: Predictive Accuracy (%) across different Models

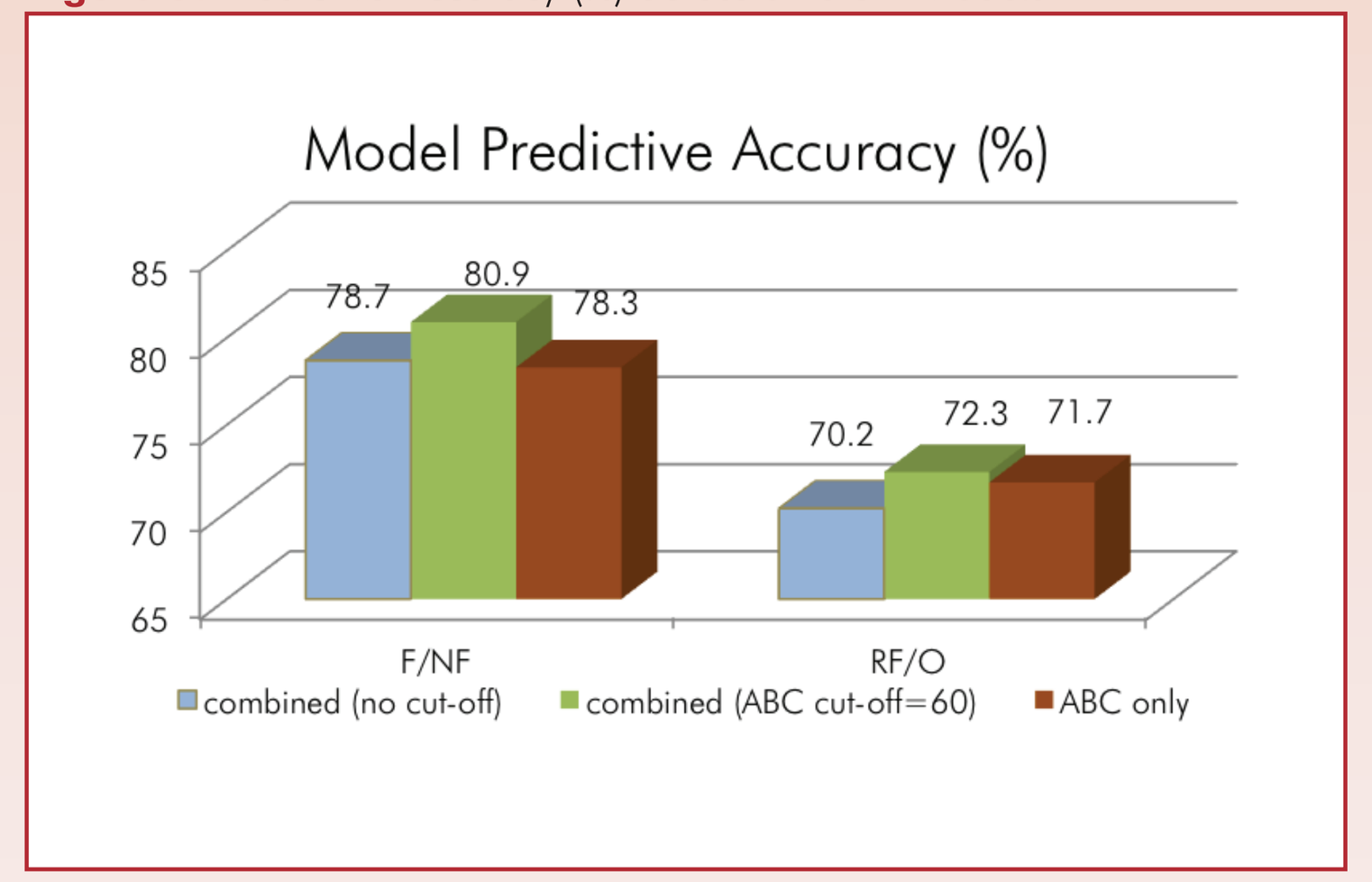


Figure 6: Cut-off determination for ABC (Fallers vs. Non-fallers)

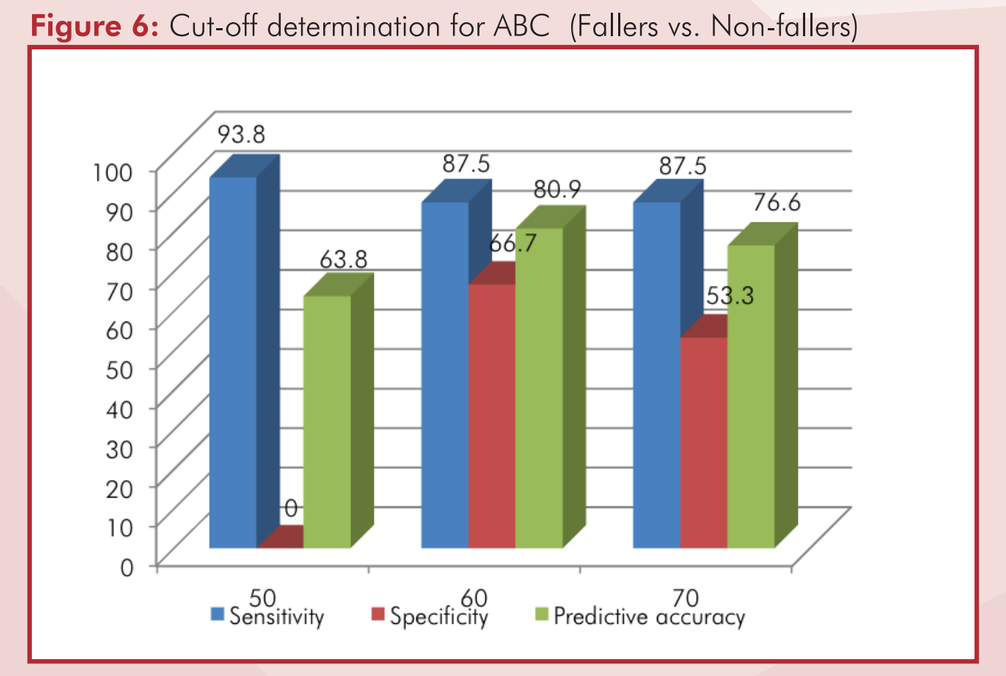
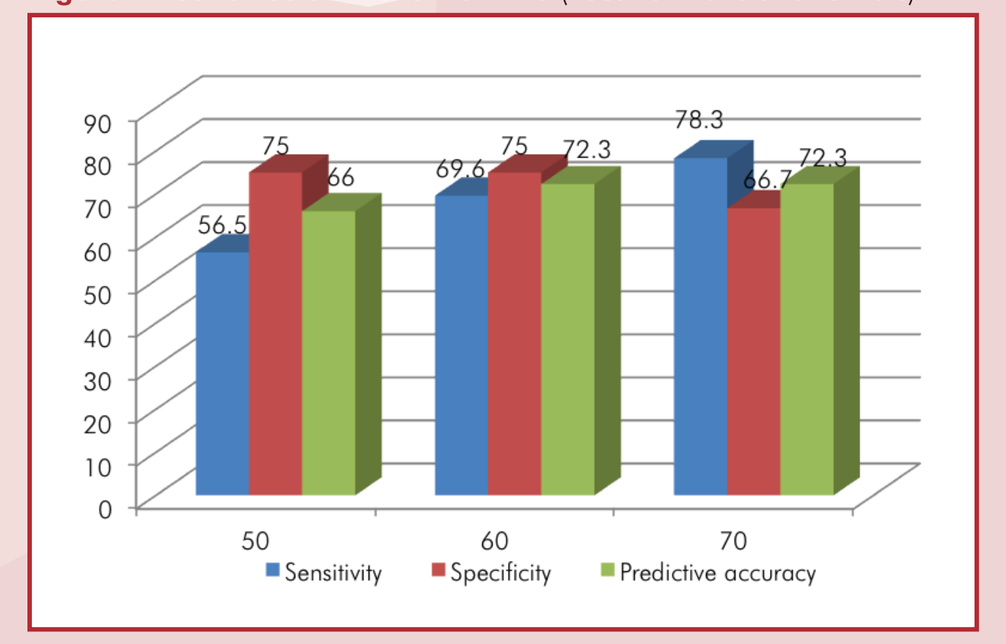


Figure 7: Cut-off determination for ABC (Recurrent fallers vs. Others)



Limitations

- Cross-sectional design with retrospective fall history.
- Small sample size.
- Selection of a convenience sample.

Conclusions

- Concurrent with previous literature, our sample depicted a high incidence (61.8%) of falls in PwMS, with a reported recurrence of 73.5%.
- Poor self-reported balance confidence, higher levels of spasticity and poor cognition resulted in a significantly higher number of falls in PwMS.
- Probability of determining a faller from a non-faller was significantly higher in people with low self-reported balance, higher spasticity and low cognition. Although not significant, a similar trend was noted in the recurrent fallers.
- The cut-off score of 60 on ABC achieved model significance and improvements in sensitivity, specificity and predictive accuracy.
- Since the self-reported balance confidence emerged as a substantial predictor of falls in PwMS, a cut-off of 60 on ABC has been suggested to enhance model prediction.
- Thus these factors, respectively, should be considered vital for fall-risk screening and fall-intervention programs.

References

1. Finlayson, M.L., Peterson, E.W., Cho, C.C. (2006). Risk factors for falling among people aged 45 to 90 years with multiple sclerosis. Arch Phys Med Rehabil, 87, 1274-9.
2. Nilsagård, Y., Lundholm, C., Denison, E., Gunnarsson, L-G. (2009). Predicting accidental falls in people with multiple sclerosis - a longitudinal study. Clin Rehabil, 23, 259-269.