Supplementary_S3 Table S1. Comparison between «a priori» vs «data driven» estimated scores (pooled analysis in 677 NP 1st events).

Item	CATEGORY	A PRIORI ORIGINAL COEFFICIENTS*	DATA DRIVEN (REFINED A POSTERIORI) COEFFICIENTS
Time onset of NP event	Before	**0**	0
	After	**2**	2.1
	Concurrent	**3**	3.1
Minor event (Ainiala list)	Yes	**0**	0
	No	**3**	2.9
Presence of Confounding Factors	≥ 1	**0**	0
	1	**1**	0.7
	No	**2**	1.9
Presence of favouring factors	No	**0**	0
	1	**1**	0.9
	≥ 1	**2**	2.1

(^) The resulting global score can range from 0 to 10; details for definition of each item category are reported elsewhere (9).
*A priori coefficients (original coefficients), identify the better scores to be used in the final version of the Italian attribution algorithm, the so-called “original algorithm” (^)

Supplementary_S3 Table S2. ROC curve analysis related to the following NP event observed in the international cohort, stratified by all subsequent events and in relation to the first event (related or unrelated).

Subsequent event	N° of events	AUC	[95% Conf. Interval]
All	93	0.80	(0.71 – 0.88)
After a 1st unrelated NP event	33	0.83	(0.68 – 0.97)
After a 1st related NP event	60	0.79	(0.68 – 0.91)

Supplementary_S3 Table S3. Detailed report of sensitivity, specificity, PPV and NPV for each defined cut-point derived from the application of the attribution algorithm to the first NP event observed in the training (cohort 1), validating (cohort 2) and pooled cohorts (all three cohorts, including the international cohort).

Cohort	Cut-point	Sensitivity	Specificity	Correctly Classified	LR+	LR-	PPV	NPV
1	(>= 0)	100.00%	0.00%	62.67%	100.00%		62.67%	
1	(>= 1)	100.00%	0.00%	62.67%	1		62.67%	
1	(>= 2)	100.00%	1.19%	63.11%	1.012	0	62.95%	100.00%
1	(>= 3)	99.29%	7.14%	64.89%	1.0693	0.0993	64.22%	85.70%
1	(>= 4)	99.29%	16.67%	68.44%	1.1915	0.0426	66.67%	93.33%
1	(>= 5)	95.74%	35.71%	73.33%	1.4894	0.1191	71.43%	83.32%
1	**(>= 6)**	85.11%	61.90%	**76.44%**	2.234	0.2406	78.95%	71.24%
1	(>= 7)	58.87%	92.86%	71.56%	8.2411	0.443	93.26%	57.36%
1	(>= 8)	36.17%	100.00%	60.00%	0.6383		100.00%	48.28%
1	(>= 9)	21.99%	100.00%	51.11%	0.7801		100.00%	43.30%
1	(>= 10)	6.38%	100.00%	41.33%	0.9362		100.00%	
1	(> 10)	0.00%	100.00%	37.33%	1			

Cohort	Cut-point	Sensitivity	Specificity	Correctly Classified	LR+	LR-	PPV	NPV
2	(>= 0)	100.00%	0.00%	51.20%	1		51.20%	
2	(>= 1)	100.00%	0.00%	51.20%	1		51.20%	
2	(>= 2)	100.00%	0.98%	51.67%	1.0099	0	51.44%	100.00%
2	(>= 3)	97.20%	5.88%	52.63%	1.0327	0.4766	52.00%	66.69%
2	(>= 4)	96.26%	17.65%	57.89%	1.1689	0.2118	55.08%	81.81%
2	(>= 5)	91.59%	36.27%	64.59%	1.4372	0.2319	60.12%	80.44%
2	(>= 6)	85.98%	61.76%	74.16%	2.2487	0.227	70.23%	80.77%
2	**(>= 7)**	71.96%	80.39%	**76.08%**	3.6701	0.3488	79.38%	73.21%
2	(>= 8)	58.88%	92.16%	75.12%	7.507	0.4462	88.74%	68.12%
2	(>= 9)	32.71%	95.10%	63.16%	6.6729	0.7076	87.50%	57.40%
2	(>= 10)	10.28%	98.04%	53.11%	5.243	0.9151	84.62%	51.02%
2	(> 10)	0.00%	100.00%	48.80%	1			48.80%

Cohort	Cut-point	Sensitivity	Specificity	Correctly Classified	LR+	LR-	PPV	NPV
pooled	(>= 0)	100.00%	0.00%	51.26%	1		51.26%	
pooled	(>= 1)	100.00%	0.91%	51.70%	1.0092	0	51.48%	100.00%
pooled	(>= 2*)	99.71%	3.33%	52.73%	1.0315	0.0865	52.03%	91.61%
pooled	(>= 3)	98.56%	10.91%	55.83%	1.1063	0.1321	53.77%	87.81%
pooled	(>= 4)	97.41%	23.64%	61.45%	1.2756	0.1097	57.29%	89.67%
pooled	(>= 5)	93.66%	41.52%	68.24%	1.6014	0.1527	62.74%	86.17%
pooled	(>= 6)	87.32%	66.06%	76.96%	2.5728	0.1919	73.01%	83.21%
pooled	(>= 7)	71.18%	84.55%	77.70%	4.6059	0.3409	82.89%	73.61%
pooled	(>= 8*)	52.74%	93.64%	72.67%	8.2874	0.5047	89.71%	65.33%
pooled	(>= 9)	32.56%	97.27%	64.11%	11.9404	0.6933	92.62%	57.84%
pooled	(>= 10)	11.24%	99.09%	54.06%	12.3631	0.8958	92.85%	51.50%
pooled	(> 10)	0.00%	100.00%	48.74%	1			48.74%

*Cut points ensuring a misclassification probability less than 10%