

**Table e-1. Association between pseudobulbar affect (PBA) and disease and multiple sclerosis (MS) symptom severity.**PBA defined as CNS-LS  $\geq 17$  with no current depression<sup>¥</sup> (200 cases of PBA)

	No. of patients in each category			Moderate vs. Mild*	Severe vs. Mild	Per 1 point increase in score**
	Mild	Moderate	Severe	Odds Ratio* (95% CI)	Odds Ratio (95% CI)	Odds Ratio (95% CI)
PDDS <sup>o</sup>	53/2271	79/2598	67/3021	1.42 (0.98-2.06)	1.13 (0.75-1.70)	1.10 (0.86-1.40)
Mobility	61/2465	88/3254	44/2162	1.20 (0.85-1.70)	0.93 (0.60-1.44)	1.09 (0.85-1.39)
Hand	97/4466	76/2583	25/839	<b>1.37 (1.01-1.87)</b>	1.48 (0.93-2.35)	<b>1.42 (1.11-1.83)</b>
Vision	112/5184	76/2393	9/309	<b>1.41 (1.04-1.91)</b>	1.26 (0.63-2.54)	<b>1.36 (1.06-1.75)</b>
Fatigue	47/2097	108/3811	41/2019	1.21 (0.86-1.72)	0.84 (0.54-1.29)	0.91 (0.72-1.17)
Cognition	94/4467	91/2944	14/514	<b>1.37 (1.01-1.84)</b>	1.18 (0.67-2.11)	<b>1.44 (1.12-1.84)</b>
Spasticity	87/4259	88/2758	25/895	<b>1.49 (1.10-2.03)</b>	1.31 (0.82-2.08)	<b>1.44 (1.12-1.84)</b>
Sensory	107/4559	70/2521	23/846	1.12 (0.82-1.54)	1.10 (0.69-1.76)	1.12 (0.87-1.45)

PBA defined as CNS-LS  $\geq 17$  adjusted for depression severity (574 cases of PBA)

	No. of patients in each category			Moderate vs. Mild	Severe vs. Mild	Per 1 point increase in score
	Mild	Moderate	Severe	Odds Ratio <sup>†</sup> (95% CI)	Odds Ratio <sup>†</sup> (95% CI)	Odds Ratio (95% CI) <sup>‡</sup>
PDDS <sup>o</sup>	106/2218	254/2423	213/2875	<b>1.36 (1.05-1.77)</b>	1.16 (0.88-1.52)	1.08 (0.93-1.25)
Mobility	125/2401	313/3029	131/2075	<b>1.34 (1.06-1.71)</b>	0.99 (0.74-1.32)	1.08 (0.93-1.27)
Hand	204/4359	266/2393	99/765	<b>1.60 (1.31-1.97)</b>	<b>1.80 (1.36-2.38)</b>	<b>1.47 (1.26-1.73)</b>
Vision	240/5056	279/2190	50/268	<b>1.68 (1.39-2.04)</b>	<b>1.92 (1.34-2.74)</b>	<b>1.62 (1.38-1.90)</b>
Fatigue	65/2079	267/3652	241/1819	1.33 (0.99-1.80)	<b>1.48 (1.07-2.05)</b>	<b>1.18 (1.01-1.38)</b>
Cognition	154/4407	313/2722	106/422	<b>1.72 (1.38-2.14)</b>	<b>2.77 (2.04-3.75)</b>	<b>1.87 (1.59-2.19)</b>
Spasticity	180/4166	279/2567	111/809	<b>1.56 (1.27-1.92)</b>	<b>1.66 (1.26-2.18)</b>	<b>1.43 (1.28-1.69)</b>
Sensory	193/4473	245/2346	135/734	<b>1.49 (1.21-1.84)</b>	<b>2.17 (1.68-2.82)</b>	<b>1.59 (1.36-1.87)</b>

PBA defined as CNS-LS  $\geq 17$  unadjusted for depression severity (574 cases of PBA)

	No. of patients in each category			Moderate vs. Mild	Severe vs. Mild	Per 1 point increase in score
	Mild	Moderate	Severe	Odds Ratio* (95% CI)	Odds Ratio (95% CI)*	Odds Ratio (95% CI)**
PDDS <sup>o</sup>	106/2218	254/2423	213/2875	<b>2.15 (1.68-2.75)</b>	<b>1.77 (1.37-2.31)</b>	<b>1.36 (1.17-1.57)</b>
Mobility	125/2401	313/3029	131/2075	<b>2.05 (1.64-2.58)</b>	<b>1.42 (1.08-1.87)</b>	<b>1.38 (1.19-1.60)</b>
Hand	204/4359	266/2393	99/765	<b>2.36 (1.94-2.87)</b>	<b>2.96 (2.27-3.86)</b>	<b>2.26 (1.94-2.63)</b>
Vision	240/5056	279/2190	50/268	<b>2.53 (2.10-3.04)</b>	<b>3.68 (2.62-5.17)</b>	<b>2.50 (2.14-2.92)</b>
Fatigue	65/2079	267/3652	241/1819	<b>2.28 (1.72-3.02)</b>	<b>3.94 (2.96-2.56)</b>	<b>2.35 (2.02-2.74)</b>
Cognition	154/4407	313/2722	106/422	<b>2.96 (2.42-3.63)</b>	<b>6.35 (4.83-8.37)</b>	<b>3.53 (3.02-4.13)</b>
Spasticity	180/4166	279/2567	111/809	<b>2.39 (1.96-2.92)</b>	<b>3.06 (2.36-3.96)</b>	<b>2.30 (1.97-2.68)</b>

Sensory	193/4473	245/2346	135/734	<b>2.32 (1.90-2.83)</b>	<b>4.13 (3.24-5.26)</b>	<b>2.66 (2.28-3.11)</b>
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¥More stringent definition for PBA[+] (CNS-LS scores  $\geq 17$  and no depression; n=200)

<sup>o</sup>PDSS: Patient-derived disease steps

\*from multinomial model adjusted for age, symptom duration (quartiles), sex, race (Caucasian, African-American, Other), and income (<\$30,000, \$30,000-\$50,000,  $\geq \$50,000$ , I prefer not to answer)

\*\*from proportional odds model adjusted for age, symptom duration (quartiles), sex, race (Caucasian, African-American, Other), and income (<\$30,000, \$30,000-\$50,000,  $\geq \$50,000$ , I prefer not to answer)

<sup>†</sup>from multinomial model adjusted for depression severity, age, symptom duration (quartiles), sex, race (Caucasian, African-American, Other), and income (<\$30,000, \$30,000-\$50,000,  $\geq \$50,000$ , I prefer not to answer)

<sup>‡</sup>from proportional odds model adjusted for depression severity, age, symptom duration (quartiles), sex, race (Caucasian, African-American, Other), and income (<\$30,000, \$30,000-\$50,000,  $\geq \$50,000$ , I prefer not to answer)