

Supplementary Material

Sex, Neuropsychiatric Profiles, and Caregiver Burden in Alzheimer's Disease Dementia: A Latent Class Analysis

Supplementary Table 1. Neuropsychiatric symptoms and caregiver burden: Adjusted analysis

Neuropsychiatric symptom	N	%	beta coefficient*	95%CI*	p*
agitation/aggression	122	11.5%	1.97	(-1.21 to 5.14)	0.22
hallucinations	95	8.9%	3.62	(0.22 to 7.03)	0.04
anxiety	528	49.6%	-0.58	(-2.51 to 1.36)	0.56
apathy/indifference	677	63.6%	-0.40	(-2.29 to 1.50)	0.68
aberrant motor behavior	73	6.9%	2.64	(-0.95 to 6.23)	0.15
delusions	197	18.5%	3.44	(0.86 to 6.01)	0.01
depression/dysphoria	429	40.3%	2.89	(0.86 to 4.91)	0.01
disinhibition	72	6.8%	5.52	(1.85 to 9.18)	<0.01 [†]
elation/euphoria	14	1.3%	1.41	(-6.56 to 9.37)	0.73
appetite and eating disorders	154	14.5%	1.99	(-0.60 to 4.59)	0.13
irritability/lability	565	53.1%	2.46	(0.56 to 4.36)	0.01
sleep and night-time behaviors	303	28.5%	2.10	(0.00 to 4.20)	0.05

*Estimates obtained from a multivariable linear regression model with Zarit Burden Interview scores as dependent variable and the following covariates: age (patient/caregiver), sex (patient/caregiver), education (patient/caregiver), CDR, MMSE, and dementia subtype (probable/possible).

[†]Statistically significant p-values after Bonferroni correction (p<0.004)

Supplementary Table 2. Neuropsychiatric symptoms and caregiver burden by patient's sex: Adjusted analyses

Neuropsychiatric symptom	Male patients					Female patients				
	N	%	beta*	95%CI*	p*	N	%	beta*	95%CI*	p*
agitation/aggression	52	12.5%	4.69	(-0.14 to 9.52)	0.06	70	10.8%	0.32	(-3.96 to 4.60)	0.88
hallucinations	25	6.0%	2.64	(-3.81 to 9.09)	0.42	70	10.8%	4.56	(0.49 to 8.62)	0.03
anxiety	178	42.7%	-2.33	(-5.53 to 0.87)	0.15	350	54.0%	0.44	(-2.06 to 2.94)	0.73
apathy/indifference	272	65.2%	-2.45	(-5.60 to 0.69)	0.13	405	62.5%	1.27	(-1.14 to 3.68)	0.3
aberrant motor behavior	24	5.8%	4.17	(-2.16 to 10.49)	0.2	49	7.6%	1.16	(-3.32 to 5.64)	0.61
delusions	60	14.4%	5.02	(0.44 to 9.59)	0.03	137	21.1%	2.74	(-0.41 to 5.90)	0.09
depression/dysphoria	136	32.6%	4.42	(1.15 to 7.69)	0.01	293	45.2%	1.89	(-0.71 to 4.50)	0.15
disinhibition	38	9.1%	3.74	(-1.49 to 8.98)	0.16	34	5.2%	7.9	(2.58 to 13.22)	<0.01
elation/euphoria	9	2.2%	0.28	(-9.92 to 10.48)	0.96	5	0.8%	1.85	(-11.43 to 15.13)	0.78
appetite and eating disorders	39	9.4%	-1.78	(-6.74 to 3.19)	0.48	115	17.7%	3.76	(0.66 to 6.86)	0.02
irritability/lability	230	55.2%	2.40	(-0.70 to 5.49)	0.13	335	51.7%	2.82	(0.39 to 5.26)	0.02
sleep and night-time behaviors	117	28.1%	3.36	(-0.03 to 6.75)	0.05	186	28.7%	1.52	(-1.22 to 4.26)	0.28

* Estimates obtained from sex-specific multivariable linear regression models with Zarit as dependent variable and the following covariates: age (patient/caregiver), sex (caregiver), education (patient/caregiver), CDR, MMSE, and dementia subtype (probable/possible).

No statistically significant p-values after Bonferroni correction ($p < 0.002$)

Supplementary Table 3. Patient characteristics by NPS profiles: pairwise class comparisons

Factors	class 1	class 2	class 3	class 4	class 5	Pairwise class comparisons									
	<i>Affective</i>	<i>High behavioral disturbance</i>	<i>Negative affect</i>	<i>Affective/deliriant</i>	<i>Apathy</i>	1 vs. 2	1 vs. 3	1 vs. 4	1 vs. 5	2 vs. 3	2 vs. 4	2 vs. 5	3 vs. 4	3 vs. 5	4 vs. 5
	N=387	N=35	N=110	N=122	N=411										
Sex															
male	135 (34.9%)	11 (31.4%)	56 (50.9%)	35 (28.7%)	180 (43.8%)	0.68	<0.01	0.21	0.01	0.04	0.75	0.16	<0.001*	0.18	<0.01
female	252 (65.1%)	24 (68.6%)	54 (49.1%)	87 (71.3%)	231 (56.2%)										
Age categories															
40-59	9 (2.3%)	0 (0.0%)	3 (2.7%)	3 (2.5%)	10 (2.4%)	<0.001*	<0.001*	0.08	0.05	0.31	0.03	0.02	0.06	0.03	0.87
60-69	35 (9.0%)	2 (5.7%)	4 (3.6%)	7 (5.7%)	32 (7.8%)										
70-79	137 (35.4%)	3 (8.6%)	19 (17.3%)	40 (32.8%)	122 (29.7%)										
80-89	188 (48.6%)	22 (62.9%)	71 (64.5%)	58 (47.5%)	207 (50.4%)										
90+	18 (4.7%)	8 (22.9%)	13 (11.8%)	14 (11.5%)	40 (9.7%)										
Mean (SD)	79.0 (7.9)	84.7 (6.2)	82.1 (7.5)	80.6 (8.0)	80.1 (7.9)	<0.001*	<0.001*	0.06	0.06	0.06	0.01	<0.001	0.15	0.02	0.53
Education															
primary or less	156 (40.3%)	14 (40.0%)	44 (40.0%)	55 (45.1%)	155 (37.7%)	0.97	0.95	0.35	0.45	1.00	0.59	0.79	0.43	0.66	0.14
secondary or more	231 (59.7%)	21 (60.0%)	66 (60.0%)	67 (54.9%)	256 (62.3%)										
CDR															
1	211 (54.5%)	8 (22.9%)	42 (38.2%)	32 (26.2%)	188 (45.7%)	<0.001*	0.01	<0.001*	<0.01	0.13	0.74	0.02	0.13	0.27	<0.001
2	160 (41.3%)	21 (60.0%)	59 (53.6%)	75 (61.5%)	185 (45.0%)										
3	16 (4.1%)	6 (17.1%)	9 (8.2%)	15 (12.3%)	38 (9.2%)										
MMSE															
Mean (SD)	18.4 (4.9)	13.9 (5.8)	16.5 (5.4)	15.6 (5.3)	17.1 (5.9)	<0.001*	<0.001*	<0.001*	<0.01	0.02	0.10	<0.01	0.25	0.28	0.01
Dementia subtypes															
possible	127 (32.8%)	17 (48.6%)	20 (18.2%)	41 (33.6%)	99 (24.1%)	0.06	<0.01	0.87	0.01	<0.001*	0.11	<0.01	0.01	0.19	0.04
probable	260 (67.2%)	18 (51.4%)	90 (81.8%)	81 (66.4%)	312 (75.9%)										

* Statistically significant p-values after Bonferroni correction (p<0.0006)

Supplementary Table 4. Caregiver characteristics by NPS profiles: pairwise class comparisons

Factors	class 1	class 2	class 3	class 4	class 5	Pairwise class comparisons									
	<i>Affective</i>	<i>High behavioral disturbance</i>	<i>Negative affect</i>	<i>Affective/deliriant</i>	<i>Apathy</i>	1 vs. 2	1 vs. 3	1 vs. 4	1 vs. 5	2 vs. 3	2 vs. 4	2 vs. 5	3 vs. 4	3 vs. 5	4 vs. 5
	N=387	N=35	N=110	N=122	N=411										
Sex															
male	168 (43.4%)	8 (22.9%)	20 (18.2%)	42 (34.4%)	157 (38.2%)	<0.001*	0.02	<0.001*	0.08	0.13	0.54	0.20	0.07	0.01	<0.001*
female	219 (56.6%)	27 (77.1%)	90 (81.8%)	80 (65.6%)	254 (61.8%)										
Age categories															
30-59	93 (24.0%)	9 (25.7%)	25 (22.7%)	41 (33.6%)	82 (20.0%)	0.23	0.15	0.99	0.20	0.58	0.39	0.44	0.14	0.43	0.88
60-69	86 (22.2%)	13 (37.1%)	27 (24.5%)	29 (23.8%)	91 (22.1%)										
70-79	123 (31.8%)	7 (20.0%)	35 (31.8%)	33 (27.0%)	136 (33.1%)										
80-89	82 (21.2%)	5 (14.3%)	22 (20.0%)	18 (14.8%)	96 (23.4%)										
90+	3 (0.8%)	1 (2.9%)	1 (0.9%)	1 (0.8%)	6 (1.5%)										
Mean (SD)	68.9 (12.3)	66.3 (12.4)	69.2 (12.2)	65.4 (12.4)	70.3 (11.4)	<0.01	0.23	0.84	0.01	0.10	0.23	0.69	0.05	0.02	0.37
Education															
primary or less	226 (58.4%)	21 (60.0%)	79 (71.8%)	74 (60.7%)	254 (61.8%)	0.16	0.85	0.01	0.66	0.33	0.19	0.94	0.83	0.07	0.05
secondary or more	161 (41.6%)	14 (40.0%)	31 (28.2%)	48 (39.3%)	157 (38.2%)										

* Statistically significant p-values after Bonferroni correction (p<0.0012)

Supplementary Table 5. Likelihood of having a female caregiver according to patient characteristics

<i>Patient Characteristics</i>	<i>Female caregivers</i>		<i>Male caregivers</i>		<i>OR†</i>	<i>95%CI†</i>	<i>p†</i>
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>			
Sex							
Female*	269	40.1	379	95.9	1.00		
Male	401	59.9	16	4.1	60.89	(34.30-108.11)	<0.01
Age categories							
40-59*	9	1.3	16	4.1	1.00		
60-69	35	5.2	45	11.4	1.21	(0.29-5.07)	0.80
70-79	158	23.6	163	41.3	1.95	(0.53-7.22)	0.32
80-89	396	59.1	150	38.0	7.30	(1.98-26.88)	<0.01
90+	72	10.7	21	5.3	14.87	(3.69-59.90)	<0.01
Education							
primary or less*	268	40	156	39.5	1.00		
secondary or more	402	60	239	60.5	0.70	(0.49-0.99)	0.05
NPI profiles							
class 1 <i>Affective</i>	219	32.7	168	42.5	1.16	(0.78-1.70)	0.46
class 2 <i>High behavioral dist.</i>	27	4.0	8	2.0	2.56	(1.00-6.56)	0.05
class 3 <i>Negative affect</i>	90	13.4	20	5.1	2.72	(1.44-5.13)	<0.01
class 4 <i>Affective/deliriant</i>	80	11.9	42	10.6	2.14	(1.26-3.64)	<0.01
class 5 <i>Apathy*</i>	254	37.9	157	39.7	1.00		
CDR							
1*	307	45.8	174	44.1	1.00		
2	308	46.0	192	48.6	0.76	(0.49-1.18)	0.22
3	55	8.2	29	7.3	0.95	(0.40-2.27)	0.91
MMSE							
per unit	670	100	395	100	0.98	(0.94-1.03)	0.53
Dementia diagnosis							
possible*	211	31.5	93	23.5	1.00		
probable	459	68.5	302	76.5	0.85	(0.58-1.24)	0.39

*Reference category

†Estimates obtained by fitting a logistic regression model with all variables in the table.

Supplementary Table 6. NPS classes and Zarit Burden score by patient's sex

NPI profiles	N	Beta[†]	95%CI[†]	p[‡]	Interaction p[‡]
Male Patients					
class 1 <i>Affective</i>	135	1.46	(-1.82 to 4.75)	0.38	-
class 2 <i>High behavioral dist.</i>	11	16.7	(7.61 to 25.80)	<0.01	-
class 3 <i>Negative affect</i>	56	7.81	(3.38 to 12.23)	<0.01	-
class 4 <i>Affective/deliriant</i>	35	10.09	(4.61 to 15.58)	<0.01	-
class 5 <i>Apathy*</i>	180	-			
Female patients					
class 1 <i>Affective</i>	252	0.48	(-2.15 to 3.11)	0.72	0.90
class 2 <i>High behavioral dist.</i>	24	14.93	(8.70 to 21.15)	<0.01	0.38
class 3 <i>Negative affect</i>	54	2.92	(-1.45 to 7.29)	0.19	0.94
class 4 <i>Affective/deliriant</i>	87	8.48	(4.86 to 12.09)	<0.01	0.62
class 5 <i>Apathy*</i>	231	-			

*Reference category

[†]Estimates obtained by fitting a linear regression model with all variables in Table 4.

[‡]p-values from NPS class-specific-patient's sex interaction terms

Supplementary Table 7. NPS classes and Zarit Burden score by caregiver's sex

NPI profiles	N	Beta[†]	95%CI[†]	p[†]	Interaction p[‡]
<i>Male caregivers</i>					
class 1 <i>Affective</i>	168	-0.11	(-3.32 to 3.09)	0.94	-
class 2 <i>High behavioral dist.</i>	8	19.92	(9.47 to 30.37)	<0.01	-
class 3 <i>Negative affect</i>	20	2.28	(-4.53 to 9.10)	0.51	-
class 4 <i>Affective/deliriant</i>	42	8.22	(3.21 to 13.22)	<0.01	-
class 5 <i>Apathy*</i>	157	-			
<i>Female caregivers</i>					
class 1 <i>Affective</i>	219	1.45	(-1.25 to 4.15)	0.29	0.22
class 2 <i>High behavioral dist.</i>	27	14.29	(8.37 to 20.21)	<0.01	0.45
class 3 <i>Negative affect</i>	90	6.32	(2.78 to 9.86)	<0.01	0.86
class 4 <i>Affective/deliriant</i>	80	9.58	(5.80 to 13.35)	<0.01	0.47
class 5 <i>Apathy*</i>	254	-			

*Reference category

[†]Estimates obtained by fitting a linear regression model with all variables in Table 4.

[‡]p-values from NPS class-specific-caregivers sex interaction terms.

Supplementary Table 8. Zarit “burden” component as a function of patient/caregiver characteristics

Factors	N	Beta†	95%CI†	p†
<i>Patient characteristics</i>				
Sex				
Female*	648	-		
Male	417	0.08	(-1.86 to 2.01)	0.94
Age categories				
40-59*	25	-		
60-69	80	0.70	(-4.33 to 5.74)	0.78
70-79	321	1.38	(-3.34 to 6.09)	0.57
80-89	546	1.42	(-3.27 to 6.11)	0.55
90+	93	0.04	(-5.15 to 5.22)	0.99
Education				
primary education or less*	424	-		
secondary education or more	641	0.52	(-1.00 to 2.04)	0.5
NPI profiles				
class 1 <i>Affective</i>	387	0.15	(-1.41 to 1.71)	0.85
class 2 <i>High behavioral dist.</i>	35	11.69	(7.81 to 15.58)	<0.01
class 3 <i>Negative affect</i>	110	3.92	(1.56 to 6.27)	<0.01
class 4 <i>Affective/deliriant</i>	122	7.16	(4.88 to 9.43)	<0.01
class 5 <i>Apathy*</i>	411	-		
CDR				
1*	481	-		
2	500	4.40	(2.58 to 6.21)	<0.01
3	84	5.54	(1.89 to 9.19)	<0.01
MMSE				
per unit	1065	-0.05	(-0.24 to 0.14)	0.62
Dementia diagnosis				
possible*	304	-		
probable	761	-1.62	(-3.15 to -0.10)	0.04
<i>Caregiver characteristics</i>				
Sex				
Male*	395	-		
Female	670	1.80	(-0.18 to 3.78)	0.07
Age categories				
30-59*	250	-		
60-69	246	-0.14	(-2.24 to 1.96)	0.9
70-79	334	-4.50	(-6.70 to -2.30)	<0.01
80-89	223	-5.38	(-7.80 to -2.97)	<0.01
90+	12	-8.79	(-15.40 to -2.17)	0.01
Education				
primary education or less*	654	-		
secondary education or more	411	0.61	(-0.96 to 2.19)	0.45

*Reference category

†Estimates obtained by fitting a linear regression model with all variables in the table.

Supplementary Table 9. Zarit “dependence” component as a function of patient/caregiver characteristics

Factors	N	Beta†	95%CI†	p†
<i>Patient characteristics</i>				
Sex				
Female*	648	-		
Male	417	0.27	(-0.19 to 0.72)	0.25
Age categories				
40-59*	25	-		
60-69	80	0.89	(-0.30 to 2.07)	0.14
70-79	321	1.30	(0.20 to 2.41)	0.02
80-89	546	1.06	(-0.04 to 2.16)	0.06
90+	93	0.99	(-0.23 to 2.20)	0.11
Education				
primary education or less*	424	-		
secondary education or more	641	0.07	(-0.29 to 0.43)	0.7
NPI profiles				
class 1 <i>Affective</i>	387	0.36	(-0.01 to 0.72)	0.06
class 2 <i>High behavioral dist.</i>	35	1.32	(0.41 to 2.23)	<0.01
class 3 <i>Negative affect</i>	110	0.59	(0.04 to 1.15)	0.04
class 4 <i>Affective/deliriant</i>	122	0.95	(0.41 to 1.48)	<0.01
class 5 <i>Apathy*</i>	411	-		
CDR				
1*	481	-		
2	500	0.73	(0.30 to 1.15)	<0.01
3	84	0.74	(-0.12 to 1.60)	0.09
MMSE				
per unit	1065	-0.04	(-0.09 to 0.00)	0.06
Dementia diagnosis				
possible*	304	-		
probable	761	-0.35	(-0.71 to 0.01)	0.06
<i>Caregiver characteristics</i>				
Sex				
Male*	395	-		
Female	670	0.15	(-0.31 to 0.61)	0.53
Age categories				
30-59*	250	-		
60-69	246	0.17	(-0.32 to 0.67)	0.49
70-79	334	-0.85	(-1.36 to -0.33)	<0.01
80-89	223	-0.69	(-1.26 to -0.12)	0.02
90+	12	-1.32	(-2.87 to 0.23)	0.09
Education				
primary education or less*	654	-		
secondary education or more	411	0.20	(-0.17 to 0.57)	0.29

*Reference category

†Estimates obtained by fitting a linear regression model with all variables in the table.

Supplementary Table 10. Zarit "competency" component as a function of patient/caregiver characteristics

Factors	N	Beta†	95%CI†	p†
<i>Patient characteristics</i>				
Sex				
Female*	648	-		
Male	417	-0.25	(-0.82 to 0.32)	0.39
Age categories				
40-59*	25	-		
60-69	80	-0.61	(-2.09 to 0.87)	0.42
70-79	321	-1.14	(-2.53 to 0.24)	0.11
80-89	546	-1.09	(-2.46 to 0.29)	0.12
90+	93	-1.52	(-3.04 to 0.01)	0.05
Education				
primary education or less*	424	-		
secondary education or more	641	-0.24	(-0.69 to 0.20)	0.29
NPI profiles				
class 1 <i>Affective</i>	387	0.26	(-0.20 to 0.71)	0.27
class 2 <i>High behavioral dist.</i>	35	1.97	(0.83 to 3.12)	<0.01
class 3 <i>Negative affect</i>	110	0.51	(-0.18 to 1.20)	0.15
class 4 <i>Affective/deliriant</i>	122	0.79	(0.12 to 1.46)	0.02
class 5 <i>Apathy*</i>	411	-		
CDR				
1*	481	-		
2	500	0.37	(-0.16 to 0.91)	0.17
3	84	0.43	(-0.65 to 1.50)	0.44
MMSE				
per unit	1065	-0.03	(-0.08 to 0.03)	0.37
Dementia diagnosis				
possible*	304	-		
probable	761	-0.23	(-0.67 to 0.22)	0.32
<i>Caregiver characteristics</i>				
Sex				
Male*	395	-		
Female	670	0.57	(-0.01 to 1.15)	0.06
Age categories				
30-59*	250	-		
60-69	246	-0.07	(-0.68 to 0.55)	0.83
70-79	334	-0.76	(-1.40 to -0.11)	0.02
80-89	223	-0.86	(-1.57 to -0.15)	0.02
90+	12	-0.93	(-2.87 to 1.01)	0.35
Education				
primary education or less*	654	-		
secondary education or more	411	0.34	(-0.13 to 0.80)	0.15

*Reference category

†Estimates obtained by fitting a linear regression model with all variables in the table.