

Supplementary Material

Impact of Dementia-Related Behavioral Symptoms on Healthcare Resource Use and Caregiver Burden: Real-World Data from Europe and the United States

Supplementary Table 1. Regression analysis of HCRU data (other variables)

	Hospitalizations in the last 12 months (for any condition)			Hospitalizations in the last 12 months (relating to cognitive impairment)			Total consultations in the last 12 months		
	IRR	95% CI	p	IRR	95% CI	p	IRR	95% CI	p
Dementia severity									
Severe	2.28	1.84, 2.82	<0.001	4.35	2.85, 6.64	<0.001	1.18	1.04, 1.35	0.013
Moderate	1.84	1.44, 2.35	<0.001	3.29	2.12, 5.11	<0.001	1.14	1.05, 1.23	0.001
Mild	1			1			1		
CCI	1.21	1.16, 1.26	<0.001	1.12	1.03, 1.22	0.010	1.04	1.01, 1.07	0.003
Age	1.01	1.00, 1.02	0.003	0.99	0.97, 1.00	0.092	1.00	1.00, 1.01	0.096
Sex									
Male	1.14	0.92, 1.42	0.234	1.38	0.97, 1.96	0.072	1.01	0.95, 1.07	0.802
Female	1			1			1		
Region									
US	1.04	0.81, 1.34	0.771	0.61	0.38, 0.99	0.044	0.75	0.66, 0.85	<0.001
Europe	1			1			1		
Nursing home									
Yes	1.41	1.15, 1.71	0.001	1.62	1.09, 2.39	0.016	1.13	0.99, 1.29	0.068
No	1			1			1		
AD									
AD	0.81	0.66, 1.00	0.051	0.99	0.72, 1.36	0.966	0.97	0.90, 1.05	0.445
Not AD	1			1			1		
Specialty									
Geriatrician/neurologist	1.27	1.03, 1.58	0.027	2.62	1.81, 3.80	<0.001	0.81	0.72, 0.90	0.236
Psychiatrist	1.64	1.01, 2.66	0.044	4.12	2.00, 8.49	<0.001	0.90	0.77, 1.07	<0.001
PCP	1			1			1		
Current antipsychotic use									
Yes	1.51	1.06, 2.17	0.024	2.44	1.66, 3.60	<0.001	1.03	0.89, 1.18	0.718
No	1			1			1		

	Any current treatment			Current antipsychotic treatment		
	OR	95% CI	p	OR	95% CI	p
Severity						
Severe	1.03	0.79, 1.36	0.817	5.24	3.45, 7.95	<0.001
Moderate	0.39	0.33, 0.47	<0.001	2.59	1.82, 3.68	<0.001
Mild	1			1		
CCI	1.07	1.00, 1.13	0.036	0.92	0.85, 1.01	0.071
Age	1.01	1.00, 1.02	0.247	0.99	0.97, 1.00	0.088
Sex						
Male	0.96	0.84, 1.10	0.538	1.03	0.83, 1.28	0.801
Female	1			1		
Region						
US	0.68	0.54, 0.85	0.001	1.13	0.74, 1.72	0.569
Europe	1			1		
Nursing home						
Yes	1.78	1.34, 2.37	<0.001	1.02	0.73, 1.43	0.894
No	1			1		
AD						
AD	0.33	0.28, 0.39	<0.001	0.80	0.62, 1.04	0.097
Not AD	1			1		
Specialty						
Geriatrician/neurologist	0.82	0.67, 1.02	0.076	1.87	1.32, 2.64	<0.001
Psychiatrist	1.08	0.80, 1.45	0.621	2.59	1.65, 4.05	<0.001
PCP	1			1		
Current antipsychotic use						
Yes	0.03	0.14, 0.08	<0.001	–	–	–
No	1					

AD, Alzheimer's disease; CCI, Charlson Comorbidity Index; CI, confidence interval; HCRU, healthcare resource use; IRR, incidence rate ratio; OR, odds ratio; PCP, primary care physician; US, United States.

Supplementary Table 2. Regression analysis of patient QoL data (other variables)*

	EQ-5D-3L utility index			EQ-VAS			ADL – Getting in and out of bed		
	Coefficient	95% CI	p	Coefficient	95% CI	p	OR	95% CI	p
Dementia severity									
Severe	-0.34	-0.40, -0.28	<0.001	-22.38	-26.55, -18.20	<0.001	18.42	13.35, 25.41	<0.001
Moderate	-0.12	-0.16, -0.09	<0.001	-7.66	-10.16, -5.17	<0.001	3.73	2.88, 4.83	<0.001
Mild	0			0			1		
CCI	-0.003	-0.02, 0.01	0.600	-0.20	-1.10, 0.70	0.661	1.09	1.02, 1.15	0.009
Age	-0.01	-0.01, -0.01	<0.001	-0.27	-0.42, -0.12	0.001	1.04	1.03, 1.05	<0.001
Sex									
Male	0.04	0.01, 0.07	0.007	2.29	0.50, 4.08	0.012	0.90	0.76, 1.06	0.197
Female	0			0			1		
Region									
US	0.10	0.07, 0.14	<0.001	6.69	3.53, 9.86	<0.001	0.57	0.41, 0.78	0.001
Europe	0			0			1		
Nursing home									
Yes	-0.13	-0.22, -0.05	0.002	-2.38	-8.14, 3.37	0.416	2.06	1.59, 2.66	<0.001
No	0			0			1		
AD									
AD	0.01	-0.03, 0.04	0.623	-0.39	-2.78, 2.01	0.752	1.04	0.85, 1.28	0.690
Not AD	0			0			1		
Specialty									
Geriatrician/neurologist	0.05	0.004, 0.09	0.032	-2.27	-5.33, 0.80	0.148	0.80	0.63, 1.02	0.076
Psychiatrist	0.05	-0.02, 0.12	0.134	-1.11	-5.53, 3.32	0.623	0.65	0.44, 0.95	0.026
PCP	0			0			1		
Current antipsychotic use									
Yes	0.05	-0.02, 0.11	0.151	1.65	-2.31, 5.62	0.413	1.06	0.78, 1.43	0.710
No	0			0			1		

	ADL – Preparing meals/cooking food			ADL – Eating			ADL – Going to the toilet		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Dementia severity									
Severe	6.57	4.97, 8.68	<0.001	27.51	19.55, 38.72	<0.001	34.31	24.83, 47.39	<0.001
Moderate	4.37	3.69, 5.18	<0.001	3.82	2.90, 5.05	<0.001	6.15	4.74, 7.98	<0.001
Mild	1			1			1		
CCI	0.97	0.92, 1.02	0.286	1.09	1.01, 1.17	0.025	1.09	1.03, 1.15	0.005
Age	1.05	1.04, 1.06	<0.001	1.02	1.00, 1.03	0.029	1.02	1.01, 1.03	0.004
Sex									
Male	0.94	0.82, 1.06	0.307	1.03	0.86, 1.23	0.759	0.87	0.74, 1.02	0.090
Female	1			1			1		
Region									
US	0.96	0.80, 1.16	0.690	0.49	0.35, 0.69	<0.001	0.60	0.45, 0.81	0.001
Europe	1			1			1		
Nursing home									
Yes	0.72	0.54, 0.94	0.016	2.66	1.98, 3.59	<0.001	2.84	2.18, 3.69	<0.001
No	1			1			1		
AD									
AD	1.38	1.19, 1.61	<0.001	1.17	0.95, 1.45	0.148	1.20	0.98, 1.46	0.079
Not AD	1			1			1		
Specialty									
Geriatrician/neurologist	0.80	0.66, 0.97	0.021	0.73	0.56, 0.96	0.027	0.81	0.63, 1.05	0.106
Psychiatrist	0.77	0.59, 0.99	0.038	0.66	0.45, 0.96	0.028	0.70	0.51, 0.95	0.024
PCP	1			1			1		
Current antipsychotic use									
Yes	1.09	0.83, 1.45	0.531	1.20	0.90, 1.59	0.214	1.55	1.15, 2.09	0.004
No	1			1			1		

	ADL – Getting dressed			ADL – Washing/grooming			ADL – Walking		
	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Dementia severity									
Severe	25.75	18.77,	<0.001	22.58	16.34, 31.21	<0.001	18.10	12.89, 25.44	<0.001
Moderate	5.42	35.31	<0.001	6.07	5.03, 7.32	<0.001	3.44	2.58, 4.60	<0.001
Mild	1	4.44, 6.62		1			1		
CCI	1.03	0.97, 1.09	0.283	1.07	1.01, 1.13	0.031	1.16	1.09, 1.23	<0.001
Age	1.03	1.02, 1.04	<0.001	1.04	1.03, 1.05	<0.001	1.05	1.03, 1.06	<0.001
Sex									
Male	0.96	0.83, 1.11	0.601	0.99	0.86, 1.15	0.917	1.00	0.84, 1.20	0.979
Female	1			1			1		
Region									
US	0.54	0.42, 0.69	<0.001	0.40	0.30, 0.52	<0.001	0.81	0.57, 1.13	0.218
Europe	1			1			1		
Nursing home									
Yes	2.23	1.67, 2.99	<0.001	2.04	1.50, 2.77	<0.001	1.82	1.39, 2.38	<0.001
No	1			1			1		
AD									
AD	1.27	1.06, 1.53	0.011	1.20	1.00, 1.44	0.056	0.76	0.61, 0.96	0.019
Not AD	1			1			1		
Specialty									
Geriatrician/neurologist	0.71	0.57, 0.89	0.003	0.73	0.58, 0.91	0.006	0.77	0.60, 1.00	0.052
Psychiatrist	0.63	0.47, 0.86	0.003	0.73	0.54, 0.99	0.042	0.58	0.39, 0.88	0.009
PCP	1			1			1		
Current antipsychotic use									
Yes	1.44	1.12, 1.86	0.005	1.73	1.29, 2.31	<0.001	1.56	1.14, 2.15	0.006
No	1			1			1		

	ADL – Travelling out of home			ADL – Taking medication when required			Number of ADLs		
	OR	95% CI	p	OR	95% CI	p	IRR	95% CI	p
Dementia severity									
Severe	2.39	1.10, 5.15	0.148	5.44	3.98, 7.44	<0.001	2.09	2.00, 2.18	<0.001
Moderate	1.31	0.91, 1.89	0.027	3.09	2.62, 3.66	<0.001	1.53	1.48, 1.58	<0.001
Mild	1			1			1		
CCI	0.95	0.87, 1.04	0.296	0.99	0.93, 1.05	0.683	1.01	1.00, 1.02	0.008
Age	1.02	1.00, 1.04	0.108	1.03	1.02, 1.04	<0.001	1.01	1.01, 1.01	<0.001
Sex									
Male	1.15	0.90, 1.47	0.250	1.10	0.97, 1.24	0.128	1.00	0.98, 1.02	0.715
Female	1			1			1		
Region									
US	1.10	0.72, 1.71	0.653	1.06	0.86, 1.31	0.603	0.92	0.88, 0.95	<0.001
Europe	1			1			1		
Nursing home									
Yes	0.50	0.28, 0.89	0.018	0.92	0.68, 1.26	0.613	1.11	1.08, 1.15	<0.001
No	1			1			1		
AD									
AD	1.84	1.28, 2.66	0.001	1.23	1.06, 1.44	0.008	1.04	1.02, 1.07	0.002
Not AD	1			1			1		
Specialty									
Geriatrician/neurologist	2.91	1.91, 4.44	<0.001	0.94	0.79, 1.14	0.541	0.95	0.92, 0.99	0.006
Psychiatrist	2.36	1.37, 4.07	0.002	0.99	0.76, 1.29	0.933	0.93	0.89, 0.98	0.005
PCP	1			1			1		
Current antipsychotic use									
Yes	0.62	0.35, 1.12	0.113	1.52	1.09, 2.12	0.013	1.07	1.03, 1.11	<0.001
No	1			1			1		

*Proxy EQ-5D-3L and EQ-VAS completed by caregiver on patient's behalf. ADLs were reported by the physician on the patient record form. AD, Alzheimer's disease; ADL, Activities of Daily Living; CCI, Charlson Comorbidity Index; CI, confidence interval; EQ-5D-3L, EuroQol five-dimensional three-level; EQ-VAS, EuroQol Visual Analogue Scale; IRR, incidence rate ratio; OR, odds ratio; PCP, primary care physician; QoL, quality of life; US, United States.

Supplementary Table 3. Regression analysis of caregiver burden data (other variables)

	EQ-5D-3L utility index			EQ-VAS			WPAI – % impairment while working due to problem		
	Coefficient	95% CI	p	Coefficient	95% CI	p	Coefficient	95% CI	p
Dementia severity									
Severe	-0.02	-0.05, 0.01	0.212	-6.05	-9.46, -2.64	0.003	6.65	-2.38, 15.68	0.148
Moderate	-0.03	-0.06, -0.01	0.006	-3.53	-5.83, -1.24	0.001	9.28	3.41, 15.16	0.002
Mild	0			0			0		
CCI	0.001	-0.01, 0.01	0.816	-0.13	-0.85, 0.58	0.714	-1.53	-3.40, 0.33	0.106
Age	-0.003	-0.005, -0.002	<0.001	-0.05	-0.18, 0.08	0.472	-0.06	-0.39, 0.27	0.707
Sex									
Male	-0.004	-0.02, 0.02	0.666	0.21	-1.56, 1.97	0.818	-0.17	-5.07, 4.73	0.946
Female	0			0			0		
Region									
US	0.03	0.001, 0.05	0.038	6.99	4.42, 9.57	<0.001	-0.47	-6.49, 5.56	0.878
Europe	0			0			0		
Nursing home									
Yes	0.09	0.06, 0.12	<0.001	9.03	4.75, 13.31	<0.001	-10.64	-18.41, -2.87	0.008
No	0			0			0		
AD									
AD	0.0007	-0.02, 0.02	0.953	0.85	-1.39, 3.08	0.457	-3.24	-8.65, 2.18	0.240
Not AD	0			0			0		
Specialty									
Geriatrician/neurologist	-0.001	-0.03, 0.02	0.908	-1.84	-4.51, 0.82	0.175	1.35	-4.49, 7.19	0.648
Psychiatrist	0.02	-0.01, 0.05	0.217	-1.62	-6.04, 2.80	0.472	2.99	-6.49, 12.47	0.535
PCP	0			0			0		
Current antipsychotic use									
Yes	-0.01	-0.05, 0.03	0.532	-0.93	-4.74, 2.87	0.630	-0.10	-9.43, 9.22	0.983
No	0			0			0		

	WPAI – % overall work impairment due to problem			WPAI – % activity impairment due to problem			Overall ZBI score		
	Coefficient	95% CI	p	Coefficient	95% CI	p	Coefficient	95% CI	p
Dementia severity									
Severe	8.08	-1.53, 17.68	0.002	16.74	11.69, 21.78	<0.001	8.83	5.29, 12.36	<0.001
Moderate	9.98	3.55, 16.41	0.099	8.61	5.00, 12.22	<0.001	7.34	4.77, 9.91	<0.001
Mild	0			0			0		
CCI	-2.01	-3.84, -0.18	0.031	-0.25	-1.47, 0.96	0.683	-0.16	-0.90, 0.59	0.676
Age	-0.07	-0.42, 0.28	0.694	0.11	-0.10, 0.32	0.290	0.14	-0.005, 0.28	0.058
Sex									
Male	1.37	-4.02, 6.75	0.617	1.39	-1.48, 4.26	0.342	0.16	-1.76, 2.09	0.870
Female	0			0			0		
Region									
US	0.23	-6.52, 6.97	0.947	-1.77	-6.17, 2.63	0.429	-2.24	-5.53, 1.06	0.183
Europe	0			0			0		
Nursing home									
Yes	-12.93	-20.87, -4.99	0.002	-25.48	-32.66, -	<0.001	-16.01	-21.00, -11.02	<0.001
No	0			0	18.30		0		
AD									
AD	-3.72	-9.66, 2.23	0.219	1.43	-2.05, 4.91	0.420	-1.70	-4.24, 0.84	0.190
Not AD	0			0			0		
Specialty									
Geriatrician/neurologist	2.98	-3.38, 9.33	0.357	2.17	-1.75, 6.10	0.277	0.48	-2.41, 3.38	0.744
Psychiatrist	3.91	-6.31, 14.13	0.452	-0.65	-6.39, 5.09	0.825	-2.71	-6.87, 1.44	0.200
PCP	0			0			0		
Current antipsychotic use									
Yes	-1.69	-11.66, 8.27	0.738	6.66	0.86, 12.46	0.025	2.13	-1.52, 5.78	0.252
No	0			0			0		

AD, Alzheimer's disease; CCI, Charlson Comorbidity Index; CI, confidence interval; EQ-5D-3L, EuroQol five-dimensional three-level; EQ-VAS, EuroQol Visual Analogue Scale; PCP, primary care physician; US, United States; WPAI, Work Productivity and Activity Impairment; ZBI, Zarit Burden Interview.

Supplementary Table 4. Missing values

Covariates	Number missing	Percent missing
AARS & presence of behavioral symptoms & psychoses	444	6.3
Dementia severity	24	0.3
CCI	52	0.7
Patient age	6	0.1
Patient sex: Male	11	0.2
Region	0	0
Living situation	45	0.6
Type of dementia: AD	582	8.3
Physician specialty	0	0
Whether antipsychotic is currently prescribed	123	1.8
Outcomes	Number missing	Percent missing
<i>HCRU</i>		
Hospitalizations in the last 12 months (for any condition)	1	0
Hospitalizations in the last 12 months (relating to cognitive impairment)	56	0.8
Total consultations in the last 12 months	15	0.2
Any current treatment	161	2.3
Current antipsychotic treatment	161	2.3
<i>Patient QoL</i>		
EQ-5D-3L utility index	5463	77.8
EQ-VAS	5479	78
ADL – Getting in and out of bed	0	0
ADL – Preparing meals/cooking food	0	0
ADL – Eating	0	0
ADL – Going to the toilet	0	0
ADL – Getting dressed	0	0
ADL – Washing/grooming	0	0
ADL – Walking	0	0
ADL – Travelling out of home	0	0
ADL – Taking medication when required	0	0
Number of ADLs	0	0
<i>Caregiver burden</i>		
EQ-5D-3L utility index	5416	77.2
EQ-VAS	5443	77.5
WPAI - % impairment while working due to problem	6557	93.4
WPAI - % overall work impairment due to problem	6590	93.9
WPAI - % activity impairment due to problem	5473	78
Overall ZBI score	5507	78.4

AARS, agitation/aggression and related symptoms; AD, Alzheimer's disease; ADL, Activities of Daily Living; CCI, Charlson Comorbidity Index; EQ-5D-3L, EuroQol five-dimensional three-level; EQ-VAS, EuroQol Visual Analogue Scale; HCRU, healthcare resource use; QoL, quality of life; WPAI, Work Productivity and Activity Impairment; ZBI, Zarit Burden Interview.