

Supplementary Online Content

Weintraub D, Chiang C, Kim HM, et al. Association of antipsychotic use with mortality risk in patients with Parkinson disease. *JAMA Neurol*. Published online March 21, 2016. doi:10.1001/jamaneurol.2016.0031.

eTable 1. Characteristics of Study Patients by Antipsychotic Use

eTable 2. Adjusted Hazard Ratios for 180-Day Mortality in AP Users and Nonusers by Time of Death (ITT Analysis)

eTable 3. Adjusted Hazard Ratios For 180-Day Mortality by Antipsychotic by Time of Death (ITT Analysis)

eTable 4. Causes of Death in AP Users and Nonusers

eFigure. Mortality Rates in AP Users vs Nonusers

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Characteristics of Study Patients by Antipsychotic Use^a

Variable	AP Users (N=7877)		AP Nonusers (N=7877)		P value
	N	%	N	%	
Age group (years)					
50-55	103	1.3	93	1.2	.887
55-60	257	3.3	257	3.3	
60-65	383	4.9	393	5.0	
65-69	674	8.6	635	8.1	
70-74	1439	18.3	1453	18.4	
75-79	2260	28.7	2311	29.3	
80-84	1960	24.9	1963	24.9	
85+	801	10.2	772	9.8	
Female	65	0.8	65	0.8	NC ^b
Race					
White	6183	78.5	6183	78.5	NC ^b
Black	211	2.7	211	2.7	
Other	53	0.7	53	0.7	
Unknown	1430	18.2	1430	18.2	
Married	6153	78.1	5929	75.3	<.001
Time from PD diagnosis to index date					
<1 year	1465	18.6	1536	19.5	.440
1-3 years	3044	38.6	3014	38.3	
3-5 years	1812	23.0	1758	22.3	
>= 5 years	1556	19.8	1569	19.9	
New non-psychotropic medication use ^c	1574	20.0	1574	20.0	NC ^b
New psychotropic medication use ^c	1257	16.0	171	2.2	<.001
Benzodiazepine use ^d	2150	27.3	1320	16.8	<.001
Cholinesterase inhibitor use ^d	1519	19.3	818	10.4	<.001
Antidepressant use ^d	4533	57.5	3130	39.7	<.001
Opioid use ^d	2086	26.5	1982	25.2	.058
Depression diagnosis	2316	29.4	1523	19.3	<.001
Dementia diagnosis	603	7.7	603	7.7	NC ^b

© 2016 American Medical Association. All rights reserved.

Time from dementia diagnosis to index date (for dementia patients) ^e					
< 1 year	405	67.1	395	65.5	.822
1- 3 years	153	25.4	162	26.9	
>= 3 years	45	7.5	46	7.6	
Delirium diagnosis	1304	16.6	1304	16.6	NC ^b
Psychosis (other than bipolar disorder or schizophrenia)	1259	16.0	258	3.3	<.001
Any substance abuse disorder	124	1.6	119	1.5	.747
For dementia patients ^e	15	2.5	10	1.7	.312
For non-dementia patients ^f	109	1.5	109	1.5	NC ^b
Alcohol abuse disorder	45	0.6	94	1.2	<.001
Drug abuse disorder	93	1.2	39	0.5	<.001
Post-traumatic stress disorder diagnosis	417	5.3	408	5.2	.748
For dementia patients ^e	25	4.2	16	2.7	.153
For non-dementia patients ^f	392	5.4	392	5.4	NC ^b
Other anxiety disorder diagnosis	769	9.8	476	6.0	<.001
Personality disorder diagnosis	28	0.4	13	0.2	.019
Charlson Comorbidity Index					
0	4068	51.6	4068	51.6	NC ^b
1	1644	20.9	1644	20.9	
>1	2165	27.5	2165	27.5	
Diseases in Charlson Comorbidity Index					
Myocardial infarction	232	2.9	234	3.0	.925
Congestive heart failure	597	7.6	563	7.1	.300
Peripheral vascular disease	330	4.2	366	4.6	.163
Cerebrovascular disease	873	11.1	797	10.1	.049
Chronic obstructive pulmonary disease	894	11.3	1016	12.9	.003
Rheumatologic disease	91	1.2	92	1.2	.941
Peptic ulcer disease	126	1.6	120	1.5	.700
Cirrhosis	20	0.3	25	0.3	.455
Hepatic failure	5	0.1	10	0.1	.196
Diabetes mellitus	1156	14.7	1226	15.6	.120

© 2016 American Medical Association. All rights reserved.

Diabetes mellitus with complications	342	4.3	392	5.0	.059
Hemiplegia	102	1.3	98	1.2	.776
Chronic renal disease	423	5.4	498	6.3	.011
Malignant neoplasm	748	9.5	703	8.9	.215
Leukemia	45	0.6	28	0.4	.046
Lymphomas	23	0.3	19	0.2	.537
Metastatic solid tumor	41	0.5	30	0.4	.191
AIDS	10	0.1	5	0.1	.196
HIV+ without AIDS	1	<0.1	0	0.0	.317
Number non-psychiatric outpatient visits ^g					
0	638	8.1	1294	16.4	<.001
1-2	4104	52.1	4330	55.0	
3-4	1921	24.4	1460	18.5	
>=5	1214	15.4	793	10.1	
Number psychiatric outpatient visits ^g					
0	5834	74.1	6987	88.7	<.001
1	1065	13.5	450	5.7	
>1	978	12.4	440	5.6	
Neurologist visit for Parkinson's disease (past year)	2009	25.5	1423	18.1	<.001
Any hospitalization (past year)	652	8.3	652	8.3	NC ^b
Psychiatric hospitalization	36	0.5	24	0.3	.121
Non-psychiatric hospitalization	629	8.0	642	8.2	.704
Nursing home stay (past year)	186	2.4	153	1.9	.070
Days of hospitalization (past year)					
0	7225	91.7	7225	91.7	.109
1-5	232	2.9	269	3.4	
>5	420	5.3	383	4.9	
Days in nursing home (past year)					
0	7691	97.6	7724	98.1	.177
1-30	110	1.4	87	1.1	
>30	76	1.0	66	0.8	
Fiscal year of index date					

1999	245	3.11	245	3.11	NC ^b
2000	495	6.3	495	6.3	
2001	709	9.0	709	9.0	
2002	855	10.9	855	10.9	
2003	939	11.9	939	11.9	
2004	901	11.4	901	11.4	
2005	864	11.0	864	11.0	
2006	698	8.9	698	8.9	
2007	637	8.1	637	8.1	
2008	593	7.5	593	7.5	
2009	552	7.0	552	7.0	
2010	389	4.9	389	4.9	
Urban facility	7045	89.4	6905	87.7	<.001
Facility size (number of beds)					
<=200	2056	26.1	2015	25.6	.002
201-400	2036	25.8	2006	25.5	
401-600	1907	24.2	1894	24.0	
>600	1792	22.7	1815	23.0	
Academic affiliation of facility					
Low	2001	25.4	2317	29.4	<.001
Limited	2290	29.1	2137	27.1	
High	3586	45.5	3423	43.5	

^a All use and diagnostic data are based on 1 year prior to the index date unless otherwise specified.

^b NC - not computed due to matching between antipsychotic users and nonusers.

^c Within 14 days prior to index date.

^d Within 365 days prior to index date.

^e N=603 pairs for dementia group.

^f N=7274 pairs for non-dementia group.

^g Within 180 days prior to index date.

eTable 2. Adjusted Hazard Ratios for 180-Day Mortality in AP Users and Nonusers by Time of Death (ITT Analysis)

Group	Any Death (7877 pairs)		Death after 4 weeks (7699 pairs)	
	Hazard Ratio (95% CI)	<i>P</i> value*	Hazard Ratio (95% CI)	<i>P</i> value*
No AP use	1.0		1.0	
AP user	2.35 (2.08-2.66)	<.001	2.30 (2.01-2.64)	<.001
No AP use	1.0		1.0	
Atypical AP user	2.26 (1.98-2.57)	<.001	2.20 (1.90-2.55)	<.001
Typical AP user	3.65 (2.47-5.39)	<.001	3.98 (2.50-6.34)	<.001

****P* values were obtained from testing for the significance of the parameter estimates obtained from the corresponding Cox proportional hazards regression model.**

eTable 3. Adjusted Hazard Ratios For 180-Day Mortality by Antipsychotic by Time of Death (ITT Analysis)

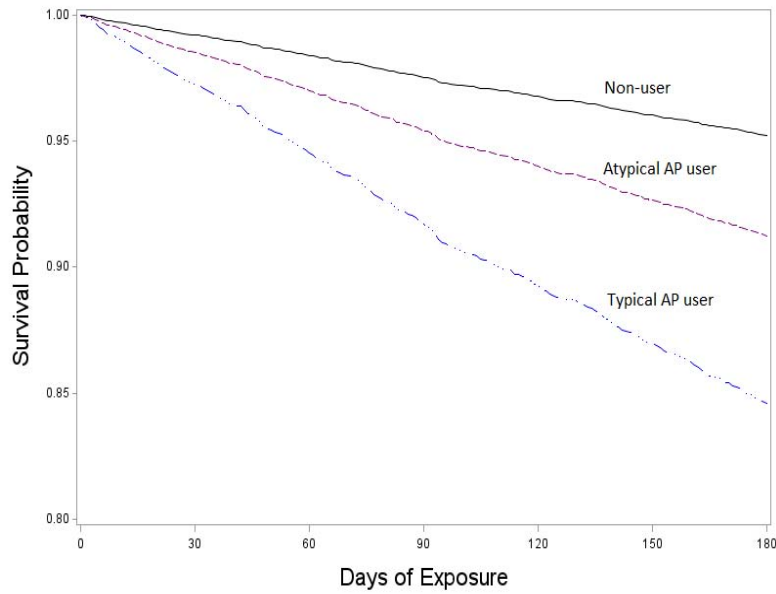
Group	Any Death (7877 pairs)		Death after 4 weeks (7699 pairs)	
	Hazard Ratio (95% CI)	<i>P</i> value*	Hazard Ratio (95% CI)	<i>P</i> value*
No AP use	1.0		1.0	
Haloperidol	5.08 (3.16-8.16)	<.001	4.34 (2.57-7.32)	<.001
Other typical AP	1.82 (0.94-3.50)	.07	3.06 (0.98-9.56)	.05
Olanzapine	2.79 (1.97-3.96)	<.001	2.48 (1.73-3.57)	<.001
Quetiapine	2.16 (1.88-2.48)	<.001	2.11 (1.80-2.47)	<.001
Risperidone	2.46 (1.94-3.12)	<.001	2.48 (1.94-3.16)	<.001
Other atypical AP	1.19 (0.60-2.37)	.62	1.48 (0.67-3.27)	.33

****P* values were obtained from testing for the significance of the parameter estimates obtained from the corresponding Cox proportional hazards regression model.**

eTable 4. Causes of Death in AP Users and Nonusers

AP users			AP nonusers		
Cause of death	No. (832)	%	Cause of death	No. (427)	%
Parkinson's disease	443	53.2	Cardiovascular diseases	246	57.6
Cardiovascular diseases	423	50.8	Parkinson's disease	165	38.6
All other diseases (residual)	313	37.6	All other diseases (residual)	164	38.4
Influenza and pneumonia	127	15.3	Malignant neoplasms	62	14.5
Clinical-Laboratory findings	110	13.2	Clinical-Laboratory findings	60	14.1
Malignant neoplasms	103	12.4	Influenza and pneumonia	57	13.3
Pneumonitis	85	10.2	Lower respiratory diseases	42	9.8
Diabetes mellitus	72	8.7	Accidents	34	8.0
Lower respiratory diseases	65	7.8	Kidney diseases	33	7.7
Other respiratory diseases	62	7.5	Septicemia	33	7.7
Kidney diseases	61	7.3	Other respiratory diseases	31	7.3
Septicemia	53	6.4	Pneumonitis	29	6.8
Accidents	45	5.4	Diabetes mellitus	27	6.3
Alzheimer's disease	40	4.8	Circulatory system disorders	12	2.8
Nutritional deficiencies	11	1.3	Alzheimer's disease	10	2.3

eFigure. Mortality Rates in AP Users vs Nonusers



	Number of patients at risk						
	0	30	60	90	120	150	180
Nonuser	7877	7698	7555	7416	7291	7170	7062
Atypical AP user	7455	7158	6856	4517	3845	2918	2557
Typical AP user	422	377	322	165	116	84	73

Covariate-adjusted 180-day survival estimates by baseline antipsychotic treatment status (exposure only). Graph is done based on Cox regression ignoring pairing.