Supplementary Material

Article Title: Antipsychotic Drugs, Mood Stabilizers, and Risk of Pneumonia in Bipolar Disorder: A Nationwide Case-Control Study

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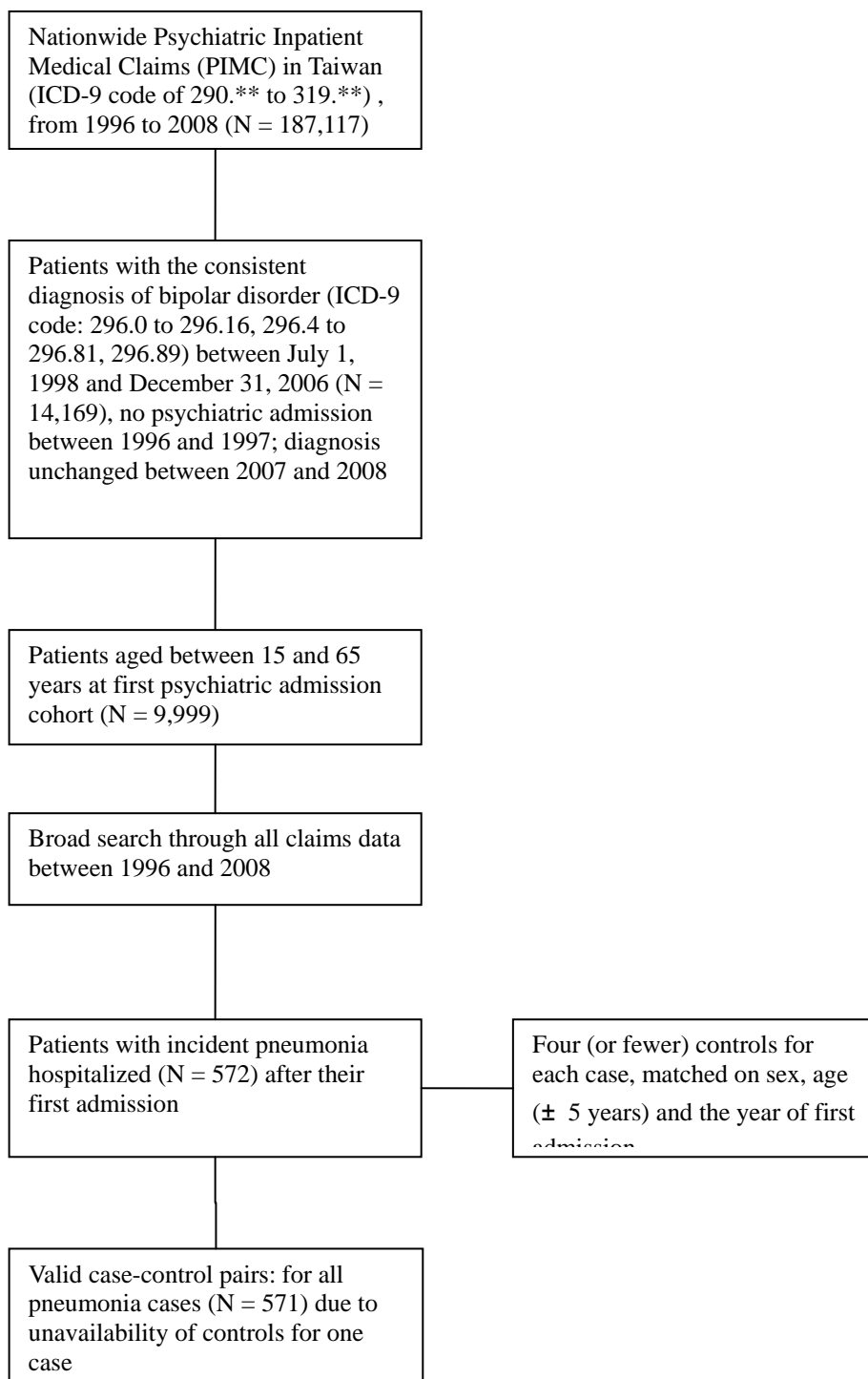
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List of Supplementary Material for the article

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Supplementary eFigure 1. Study flow diagram

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│ Nationwide Psychiatric Inpatient│
│ Medical Claims (PIMC) in Taiwan  │
│ (ICD-9 code of 290.** to 319.**),│
│ from 1996 to 2008 (N = 187,117)  │
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│ Patients with the consistent     │
│ diagnosis of bipolar disorder    │
│ (ICD-9 code: 296.0 to 296.16,    │
│ 296.4 to 296.81, 296.89) between │
│ July 1, 1998 and December 31,    │
│ 2006 (N = 14,169), no psychiatric│
│ admission between 1996 and 1997; │
│ diagnosis unchanged between 2007 │
│ and 2008                         │
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│ Patients aged between 15 and 65  │
│ years at first psychiatric       │
│ admission cohort (N = 9,999)     │
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│ Broad search through all claims  │
│ data between 1996 and 2008       │
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│ Patients with incident   │───│ Four (or fewer) controls │
│ pneumonia hospitalized   │   │ for each case, matched on│
│ (N = 572) after their    │   │ sex, age (± 5 years) and │
│ first admission          │   │ the year of first        │
│                          │   │ admission                │
└──────────────────────────┘   └──────────────────────────┘
                │
┌─────────────────────────────────┐
│ Valid case-control pairs: for all│
│ pneumonia cases (N = 571) due to │
│ unavailability of controls for   │
│ one case                         │
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Supplementary eTable 1. The distribution of mood stabilizers, second-generation and first-generation antipsychotics between the all of pneumonia cases and controls among patients with bipolar disorder (noncurrent use as the reference)

Characteristic	Pneumonia Cases (N = 571) N (%)	Controls (N = 2,277) N (%)	Propensity score-adjusted model		Multivariate adjusted model	
			Risk Ratio[a]	95% CI	Risk Ratio[b]	95% CI
Lithium						
Current use	151 (26.4)	658 (28.9)	0.75	0.57–1.00	0.75	0.56–0.99
Valproate						
Current use	225 (39.4)	701 (30.8)	1.08	0.83–1.40	1.08	0.83–1.41
Carbamazepine						
Current use	77 (13.5)	217 (9.5)	1.09	0.75–1.59	1.09	0.75–1.59
Clozapine						
Current use	45 (7.9)	51 (2.2)	2.69**	1.51–4.80	2.59*	1.46–4.63
Olanzapine						
Current use	59 (10.3)	94 (4.1)	2.97**	1.90–4.66	2.97**	1.90–4.66
Quetiapine						
Current use	98 (17.2)	219 (9.6)	2.16**	1.51–3.11	2.12**	1.48–3.03
Zotepine						
Current use	49 (8.6)	122 (5.4)	1.53	0.98–2.39	1.52	0.97–2.38
Risperidone						
Current use	83 (14.5)	212 (9.3)	1.77*	1.23–2.55	1.74*	1.21–2.50
Chlorpromazine						
Current use	39 (6.8)	125 (5.5)	1.11	0.68–1.79	1.10	0.68–1.78
Haloperidol						
Current use	203 (35.6)	316 (13.9)	3.69**	2.67–5.10	3.68**	2.66–5.09
Sulpiride						
Current use	110 (19.3)	339 (14.9)	1.28	0.94–1.75	1.29	0.94–1.76

*P < .01, **P < .001.

[a]Adjusted with the propensity score, described in the Methods.

[b]Adjusted for Charlson Comorbidity Index at the first admission, variables within 180 days before the index date listed in Table 1 (including the number of psychiatric hospital admissions, substance use disorders, physical illnesses, and concomitant medications), and the number of mood stabilizers, second- and first-generation antipsychotics.

Supplemenatry eTable 2. The distribution of second-generation antipsychotics between the pneumonia cases and controls among patients with bipolar disorder

Characteristic, N (%)	Pneumonia Cases (N = 571)	Controls (N = 2,277)	Adjusted Risk Ratio[a]	95% CI
Clozapine				
No use	476 (83.4)	2101 (92.3)	Reference	-
Past use	41 (7.2)	102 (4.5)	1.62	0.98–2.67
Recent use	9 (1.6)	23 (1.0)	1.10	0.42–2.90
Current use	45 (7.9)	51 (2.2)	2.72**	1.52–4.86
Olanzapine				
No use	436 (76.4)	1831 (80.4)	Reference	-
Past use	67 (11.7)	273 (12.0)	0.91	0.62–1.34
Recent use	9 (1.6)	79 (3.5)	0.30*	0.13–0.71
Current use	59 (10.3)	94 (4.1)	2.81**	1.78–4.44
Quetiapine				
No use	386 (67.6)	1707 (75.0)	Reference	-
Past use	63 (11.0)	247 (10.9)	1.05	0.71–1.57
Recent use	24 (4.2)	104 (4.6)	0.83	0.47–1.48
Current use	98 (17.2)	219 (9.6)	2.09**	1.43–3.06
Zotepine				
No use	434 (76.0)	1789 (78.6)	Reference	-
Past use	64 (11.2)	286 (12.6)	0.74	0.51–1.07
Recent use	24 (4.2)	80 (3.5)	1.09	0.60–1.97
Current use	49 (8.6)	122 (5.4)	1.46	0.93–2.30
Risperidone				
No use	353 (61.8)	1511 (66.4)	Reference	-
Past use	105 (18.4)	415 (18.2)	0.88	0.63–1.24
Recent use	30 (5.3)	139 (6.1)	0.87	0.52–1.47
Current use	83 (14.5)	212 (9.3)	1.67*	1.15–2.43

*$P < .01$, **$P < .001$.

[a]Adjusted for Charlson Comorbidity Index at the first admission, variables within 180 days before the index date listed in Table 1 (including the number of psychiatric hospital admissions, substance use disorders, physical illnesses, and concomitant medications), and the number of mood stabilizers, second- and first-generation antipsychotics.

Supplementary eAppendix 1. List of first- and second-generation antipsychotics and mood stabilizers included in this study

1. Antipsychotics

 a. First-generation (FGAs): haloperidol, sulpiride, chlorpromazine, flupentixol, clotiapine, zuclopenthixol, thioridazine, trifluoperazine, loxapine, levomepromazine, chlorprothixene, tiotixene, perphenazine, fluphenazine, pipotiazine, pimozide, clopenthixol, moperone

 b. Second-generation (SGAs): olanzapine, clozapine, risperidone, zotepine, quetiapine, amisulpride

2. Mood stabilizers: lithium, valproic acid, carbamazepine, topiramate, valpromide, lamotrigine, gabapentin, vigabatrin