

**SUPPLEMENTARY MATERIAL****Second-generation antipsychotics and the Risk of Chronic Kidney Disease: A Population-based Case-Control Study**

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2020

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**Appendix 1: Definitions for exposures, outcomes and confounders**

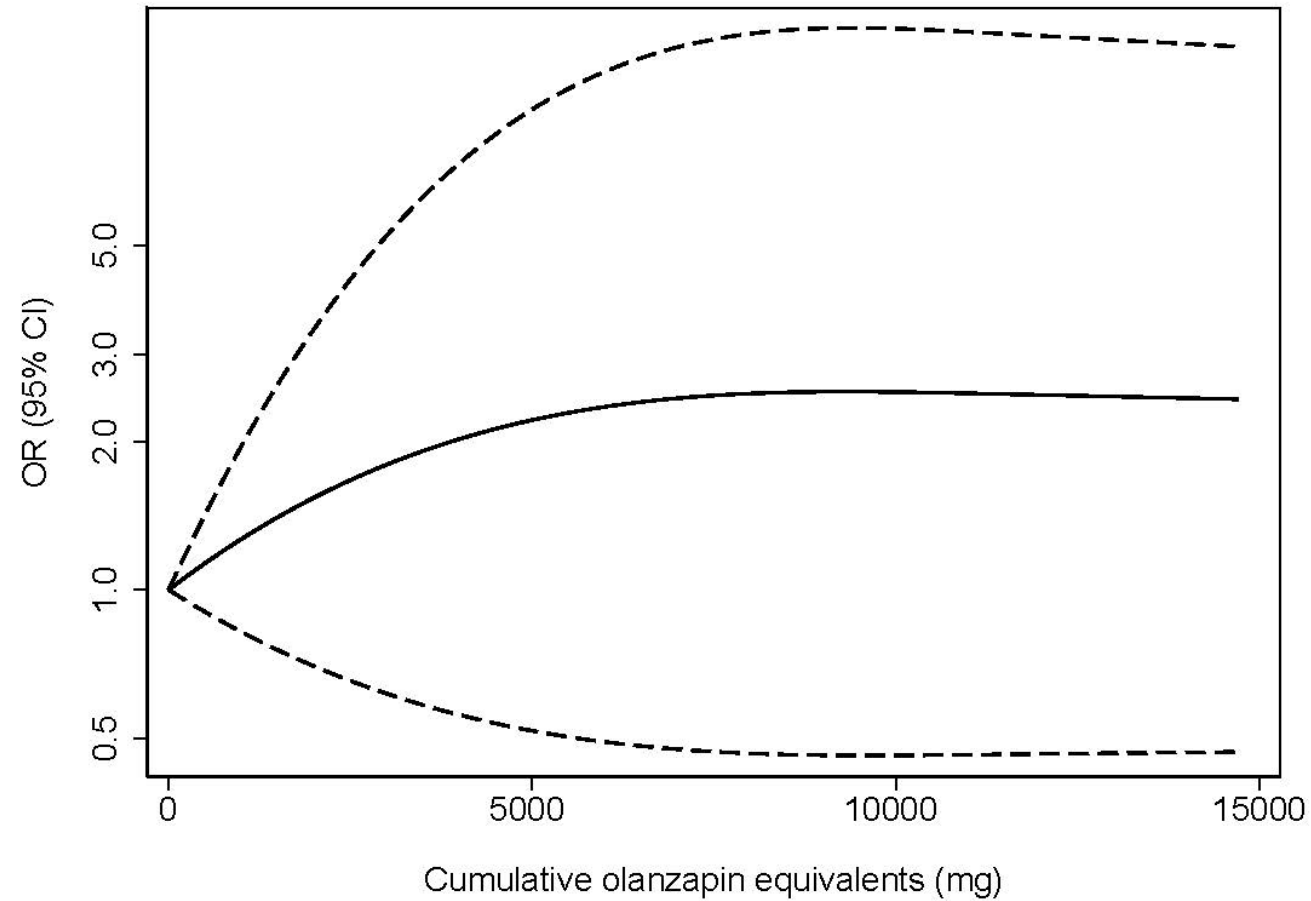
<b>Study drugs</b>	ATC code	DDD (mg)	Equivalent to 1mg olanzapine (mg)	Risk of metabolic disturbances (1)
(Second-generation antipsychotics)				
Aripiprazole	N05AX12	15	1.5	Low
Clozapine	N05AH02	300	30	High
Olanzapine	N05AH03	10	-	High
Risperidone	N05AX08	5	0.5	Mild
Quetiapine	N05AH04	400	40	Moderate
<b>Other medications</b>				
Non-steroidal anti-inflammatory drugs (NSAIDs)	M01A, excl. M01AX01			
Lithium	N05AN01			
<b>Comorbidities</b>				
	<b>Definition</b>			
Diabetes	Use of ATC-group A10			
Hypertension	Use of ATC-group C03A, C08C, C09A, C09C			
Possible CKD (2)	ICD-10: N00, 01, 03-06, 08.8, 14.1, 14.2, 16.8, 17-19, 25.1, 26-27			
Schizophrenia	ICD-10: F20			
Bipolar affective disorder	ICD-10: F30-31			
Dementia	ICD-10: F00-03 and G30-31			
Prior AKI	Defined using creatinine measurements according to Kidney Disease Improving Global Outcomes (3)			

**Appendix 2: Supplementary analysis of association between risk factors, negative control exposure and CKD**

	Crude OR (95% CI)	Adjusted OR (95% CI)
<b>Positive control exposures</b>		
History of diabetes	1.59 (1.52-1.67)	1.45 (1.38-1.52)
History of hypertension	1.56 (1.51-1.61)	1.50 (1.45-1.55)
Prior use of lithium	1.50 (1.28-1.76)	1.60 (1.36-1.87)
Recent use of NSAID	1.16 (1.12-1.20)	1.14 (1.10-1.18)
<b>Negative control exposure</b>		
Use of ocular topical antibiotics	0.95 (0.90-1.00)	0.93 (0.88-0.98)

**Appendix 3: Association between CKD and cumulated dose of SGA modeled using restricted cubic splines**

10%-percentile: 5 mg OLA eq, 50%-percentile: 250mg OLA eq, 90%-percentile: 11,200 mg OLA eq. Percentiles were derived from cumulative doses among cases. CI: Confidence interval, OLA eq: Olanzapine equivalents, OR: Odds ratio.



**Appendix 4: Sensitivity analysis with modified eligibility criteria for controls**

	Cases (N=21434)	Controls (N=85654)	Crude OR (95% CI)	Adjusted OR (95% CI)
Ever use	557	1654	1.36 (1.23-1.49)	1.27 (1.14-1.40)
Current use	399	1153	1.39 (1.24-1.56)	1.32 (1.17-1.49)
Cumulative use				
0-899mg	380	1223	1.25 (1.12-1.41)	1.17 (1.03-1.32)
900-1799mg	52	121	1.71 (1.23-2.36)	1.58 (1.13-2.21)
1800-3649mg	29	100	1.18 (0.78-1.78)	1.19 (0.78-1.83)
>3650mg	96	210	1.83 (1.44-2.34)	1.61 (1.25-2.08)
Number of prescriptions				
1-2	144	384	1.50 (1.24-1.82)	1.38 (1.13-1.69)
3-4	76	229	1.31 (1.01-1.70)	1.21 (0.93-1.59)
5-10	68	228	1.19 (0.91-1.56)	1.09 (0.83-1.45)
11-30	115	444	1.05 (0.85-1.29)	0.99 (0.80-1.22)
>30	154	369	1.69 (1.40-2.05)	1.55 (1.27-1.88)

**References**

1. De Hert M, Detraux J, van Winkel R, Yu W, Correll CU. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nat Rev Endocrinol*. 2011;8:114–26.
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3. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *KDIGO 2012 Clin Pract Guidel Eval Manag Chronic Kidney Dis*. 2013;3:1–150.