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Supplementary Material

Article Title: Comparative Effects of 30 Antipsychotics on Risk of Catatonia: An Analysis of the WHO Pharmacovigilance Database

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Supplementary Table 1: List of antipsychotics

FGA	SGA
Chlorpromazine, Levomepromazine, Promazine, Acepromazine, Triflupromazine, Cyamemazine, Chlorproethazine, Dixyrazine, Fluphenazine, Perphenazine, Prochlorperazine, Thiopropazate, Trifluoperazine, Acetophenazine, Thioproperazine, Butaperazine, Perazine, Periciazine, Thioridazine, Mesoridazine, Pipotiazine, Haloperidol, Trifluperidol, Melperone, Moperone, pipamperone, Bromperidol, Benperidol, Droperidole, Fluanisone, Molindone, Sertindole, Flupentixol, Clopenthixol, Chlorprothixene, Tiotixene, Zuclopenthixol, Fluspirilene, Pimozide, Penfluridol, Loxapine, Clotiapine, Sulpiride, Sultopride, Tiapride, Remoxipride, Veralipride, Levosulpiride, Prothipendyl, Mosapramine	Ziprasidone, Lurasidone, Clozapine, Olanzapine, Quetiapine, Asenapine, Amisulpride, Risperidone, Zotepine, Aripiprazole, Paliperidone, Iloperidone, Cariprazine, Brexiprazole

Abbreviations: FGA, First Generation of Antipsychotics; SGA, Second Generation of Antipsychotics

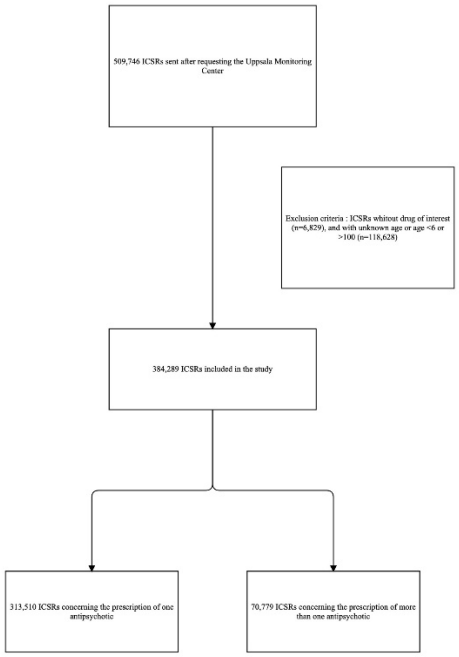
Supplementary Table 2: Number of ICSRs for each antipsychotic included in the secondary analysis

	Number of ICSRs (all adverse effects included)	Number of catatonic syndromes[a] reported	Number of catatonia OR malignant catatonia reported	Number of NMS reported
Amisulpride	2 822	85	1	82
Aripiprazole	22 944	323	37	284
Asenapine	2 480	18	.	17
Chlorpromazine	6 299	100	5	93
Clozapine	89 351	808	116	662
Cyamemazine	1 944	32	1	31
Droperidol	1 357	35	6	29
Flupentixol	1 606	40	2	38
Fluphenazine	2 073	92	10	80
Haloperidol	15 799	915	82	818
Levomepromazine	1 890	45	1	44
Loxapine	1 277	83	4	78
Lurasidone	1 638	18	2	15
Molindone	127	12	.	12
Olanzapine	32 800	737	59	664
Paliperidone	10 092	136	29	103
Periciazine	447	14	.	14
Perphenazine	1 578	38	3	35
Pimozide	564	10	1	8
Prochlorperazine	5 853	38	10	27
Quetiapine	41 756	475	48	423
Risperidone	42 598	827	82	733
Sulpiride	3 014	70	1	68
Thioridazine	2 996	75	3	71
Tiapride	1 054	46	1	45
Tiotixene	522	21	1	20
Trifluoperazine	1 599	38	1	37
Ziprasidone	4 835	113	4	104
Zotepine	213	10	1	9
Zuclopenthixol	1 468	83	3	79
TOTAL	302 996	5 337	514	4 723

Abbreviations: ICSRs: Individual Case Safety Reports NMS: Neuroleptic Malignant Syndrome

[a] By catatonic syndromes we included all ICSRs of catatonia OR malignant catatonia OR neuroleptic malignant syndrome

Supplementary Figure 1: Flowchart for the third analysis (one antipsychotic prescription versus more than one antipsychotic prescription)



Supplementary Table 3: Sensitivity analyses for the association between catatonia syndromes and the use of FGAs versus SGAs for the primary and secondary analyses

	Cases[a]	Non-Cases[b]	Crude RORs (95% CI)	Adjusted RORs (95% CI)
Restricting to 2009-2018 period				
SGA	2,015	174,533	1 (reference)	1 (reference)
FGA	745	26,767	2·4 (2·2–2·6)	2·1 (1·9–2·3)[1]
Restricting to reports from physicians				
SGA	1,540	94,836	1 (reference)	1 (reference)
FGA	650	21,288	1·9 (1·7–2·1)	1·9 (1·7–2·1)[2]
Restricting to reports from USA				
SGA	1,309	100,452	1 (reference)	1 (reference)
FGA	587	9,970	4·5 (4·1–5·0)	4·5 (4·0–4·9)[3]
Restricting to reports with a completeness score[c] > 600				
SGA	868	68,245	1 (reference)	1 (reference)
FGA	533	22,144	1·9 (1·7–2·1)	1·8 (1·6–2·0)[1]
Considering only cases of catatonia				
SGA	381	252,686	1 (reference)	1 (reference)
FGA	141	60,302	1·6 (1·3–1·9)	1·8 (1·5–2·2)[1]
Considering only cases of neuroleptic malignant syndrome				
SGA	3,100	249,967	1 (reference)	1 (reference)
FGA	1,696	58,747	2·3 (2·2–2·5)	2·2 (2·1–2·3)[1]

Abbreviations: FGA, First Generation of Antipsychotics; SGA, Second Generation of Antipsychotics

[a]: cases were reports containing all sub-terms retrieved using the MedDRA terms "Catatonia", "Malignant Catatonia" and "Neuroleptic Malignant Syndrome"

[b]: non-cases were all other reports recorded in VigiBase®

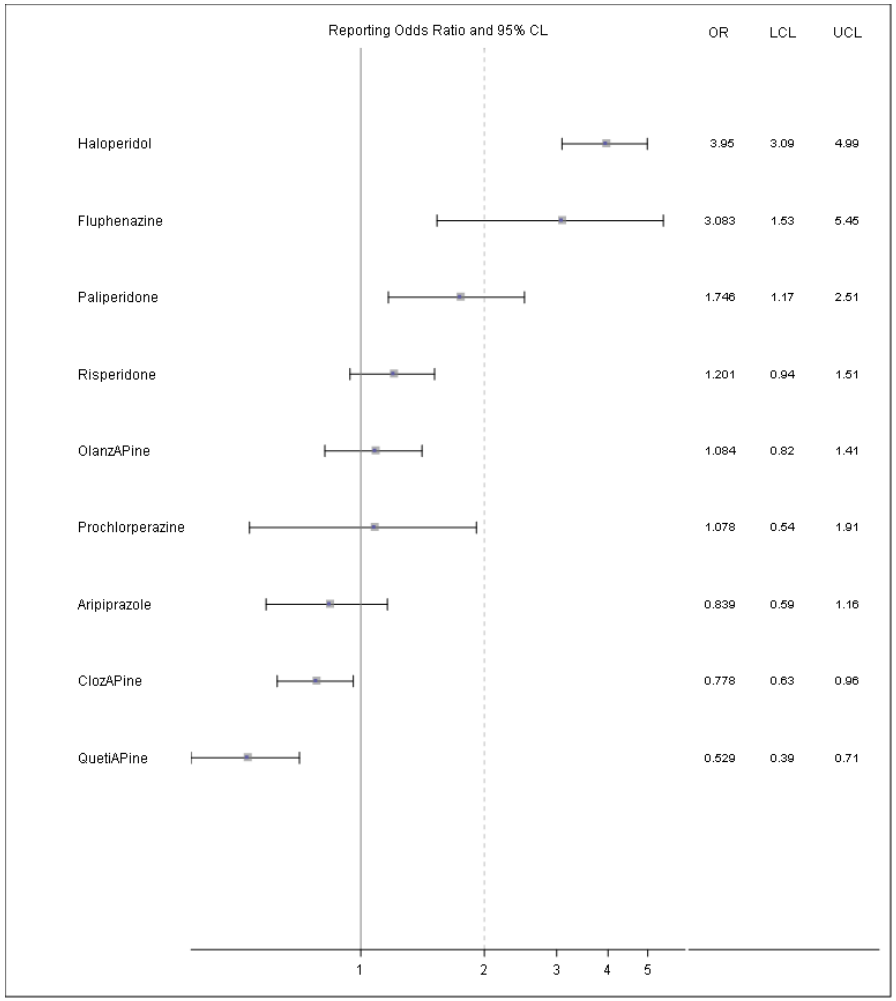
[c]: Completeness score allows to know about the level of quality of information of a report (Value ranges from 0 to 1,000)

[1]: results adjusted on age, gender, healthcare professional, USA, and number of co-prescriptions

[2]: results adjusted on age, gender, USA, and number of co-prescriptions

[3]: results adjusted on age, gender, healthcare professional and number of co-prescription

Supplementary Figure 2: Forest Plot showing adjusted RORs for the association between each antipsychotics and benign catatonia or malignant catatonia



Supplementary Figure 3: Forest Plot showing adjusted RORs for the association between each antipsychotics and Neuroleptic Malignant Syndrome