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**eAppendix 1:** Antipsychotic drugs and their Anatomical Therapeutic Chemical (ATC) classification system codes

ATC code	Antipsychotic drug
<b>First generation antipsychotic (FGA)</b>	
N05AA01	Chlorpromazine
N05AA02	Levomepromazine
N05AA03	Promazine
N05AA04	Acepromazine
N05AB02	Fluphenazine
N05AB03	Perphenazine
N05AB04	Prochlorperazine
N05AC01	Periciazine
N05AC02	Thioridazine
N05AD01	Haloperidol
N05AD05	Pipamperone
N05AD08	Droperidol
N05AF01	Flupentixol
N05AF03	Chlorprothixene
N05AF04	Tiotixene
N05AF05	Zuclopenthixol

<b>ATC code</b>	<b>Antipsychotic drug</b>
N05AG02	Pimozide
N05AG03	Penfluridol
<b>Second generation antipsychotics (SGA)</b>	
N05AD03	Melperone
N05AE03	Sertindole
N05AE04	Ziprasidone
N05AH02*	Clozapine
N05AH03*	Olanzapine
N05AH04	Quetiapine
N05AH05	Asenapine
N05AL01	Sulpiride
N05AL05	Amisulpride
N05AX08	Risperidone
N05AX12*	Aripiprazole
N05AX13	Paliperidone

\*Analysed separately

**eAppendix 2:** Risperidone, Quetiapine, and Ziprasidone related risks for Diabetes Mellitus in people with schizophrenia

	<b>IR (95%CI)</b>	<b>AHR (95%CI)</b>	<b>p value</b>
<b>Risks with starting risperidone</b>			
Before starting risperidone (n=7,600) <sup>a</sup>	3.45 (2.82-4.22)	1.00 (Reference)	-
After starting risperidone (n=2,158)	5.29 (4.14-6.76)	1.88 (1.36-2.60)	<0.001
<b>Risks with starting quetiapine</b>			
Before starting quetiapine (n=7,745) <sup>b</sup>	3.43 (2.83-4.14)	1.00 (Reference)	-
After starting quetiapine (n=2,770)	6.10 (4.85-7.67)	2.72 (2.00-3.71)	<0.001
<b>Risks with starting ziprasidone</b>			
Before starting ziprasidone (n=8,817) <sup>c</sup>	3.67 (3.12-4.32)	1.00 (Reference)	-
After starting ziprasidone (n=916)	6.54 (4.74-9.02)	2.45 (1.68-3.57)	<0.001

IR= Incidence rates of type 2 diabetes mellitus (T2DM) per 1000 person-years; AHR= Adjusted hazard ratios that were estimated by cox proportional hazard regression models. These models included gender, family history of DM, and urbanicity as time-independent covariates, and calendar period, Defined Daily Doses (DDD) of antipsychotics, DDD of valproate, and DDD of tricyclic or tetracyclic antidepressants as time-dependent covariates. <sup>a</sup> People with schizophrenia, who had received risperidone before their diagnosis of schizophrenia, were excluded from this analysis; <sup>c</sup> People with schizophrenia, who had received quetiapine before their diagnosis of schizophrenia, were excluded from this analysis; <sup>f</sup> People with schizophrenia, who had received ziprasidone before their diagnosis of schizophrenia, were excluded from this analysis.

**eAppendix 3:** Age-specific incidence rates of type 2 Diabetes Mellitus in people with (n=8,945) and without schizophrenia (2,727,565)

Age group (years)	People without schizophrenia			People with schizophrenia		
	<b>Person-years (in millions)</b>	<b>Incident T2DM (n)</b>	<b>IR (95%CI)<sup>a</sup></b>	<b>Person-years</b>	<b>Incident T2DM (n)</b>	<b>IR (95%CI)<sup>a</sup></b>
0-9	23.67	577	0.02 (0.02-0.03)	29.12	0	0.00
10-14	9.18	297	0.03 (0.03-0.04)	269.44	0	0.00
15-19	7.36	1,306	0.18 (0.17-0.19)	4,835.80	14	2.90 (1.71-4.89)
20-24	5.16	886	0.17 (0.16-0.18)	16,325.62	69	3.00 (2.27-3.97)
25-29	2.99	1,245	0.42 (0.39-0.44)	17,022.70	68	3.99 (3.15-5.07)
30-36	1.25	991	0.79 (0.74-0.84)	9,036.40	55	6.09 (4.67-7.93)
<b>0-36</b>	<b>49.61</b>	<b>5,302</b>	<b>0.11 (0.10-0.11)</b>	<b>47,519.08</b>	<b>186</b>	<b>3.91 (3.39-4.52)</b>

<sup>a</sup> Incidence rates of type 2 diabetes mellitus (T2DM) per 1000 person-years

**eAppendix 4:** Endogenous risk for type 2 Diabetes Mellitus in antipsychotic naïve people with schizophrenia

	<b>IR (95%CI)</b>	<b>AHR (95%CI)</b>	<b>p value</b>
<b>Follow-up censored at first antipsychotic prescription <sup>a</sup></b>			
People without schizophrenia (N=2,736,510) <sup>b</sup>	0.10 (0.10-0.10)	1.00 (Reference)	-
People with schizophrenia (n=4,322)	1.68 (0.93-3.03)	4.58 (2.53-8.28) <sup>c</sup>	<0.001
		4.71 (2.60-8.51) <sup>d</sup>	<0.001
<b>No use of antipsychotics during the entire follow-up <sup>e</sup></b>			
People without schizophrenia (n=2,673,114)	0.10 (0.10-0.10)	1.00 (Reference)	-
People with schizophrenia (n=1,154)	1.63 (0.73-3.62)	3.91 (1.75-8.71) <sup>c</sup>	0.001
		3.64 (1.63-8.12) <sup>d</sup>	0.002

IR= Incidence rates of type 2 diabetes mellitus (T2DM) per 1000 person-years; AHR= Adjusted Hazard Ratios that were estimated by cox proportional hazard regression models. <sup>a</sup> Data were censored at the earliest date among the following, date of diagnosis of T2DM, date of starting any antipsychotic medication, date of death, date of emigration from Denmark, and the end of follow-up on 01/01/2013; <sup>b</sup> Assuming that the people with schizophrenia were at risk for T2DM after the diagnosis of schizophrenia, analyses were carried out with reference groups including data of people without schizophrenia, and of antipsychotic naïve people with schizophrenia before the diagnosis of schizophrenia; <sup>c</sup> adjusted for the effects of gender, family history of DM, and urbanicity; <sup>d</sup> Adjusted for the effects of gender, family history of DM, urbanicity, exposure to valproate, and exposure to tricyclic or tetracyclic antidepressants; <sup>e</sup> Endogenous risk for T2DM in people with schizophrenia, who remained antipsychotic naïve until the end of follow-up, was evaluated with reference to people without schizophrenia, who have not been exposed to any antipsychotics

**eAppendix 5:** Antipsychotic-related incidence rates, and adjusted hazard ratios for type 2 Diabetes Mellitus in people with schizophrenia

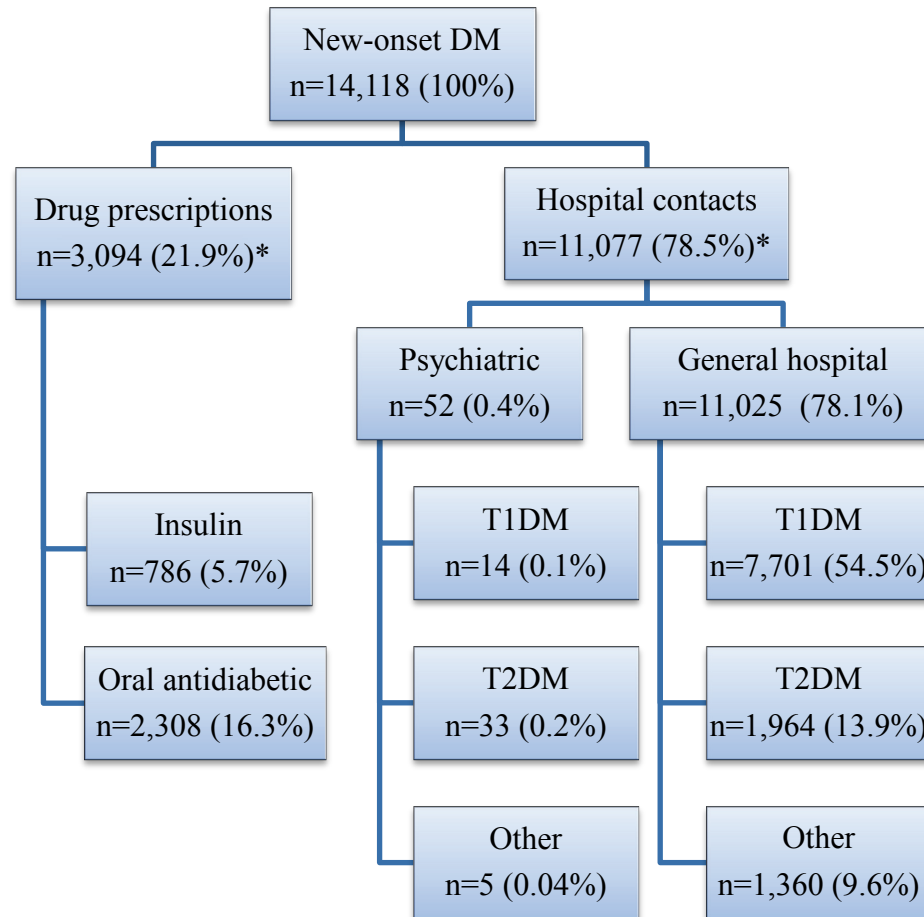
	<b>IR (95%CI)</b>	<b>AHR (95%CI)</b>	<b>p value</b>
<b>Risks with starting antipsychotics</b>			
Before starting any antipsychotic medication (n=4,322) <sup>a</sup>	1.68 (0.93-3.03)	1.00 (Reference)	-
After starting any antipsychotic medication (n=3,168)	3.70 (2.91-4.69)	3.79 (1.97-7.26)	<0.001
After first-line treatment with a FGA (n=450)	3.92 (2.23-6.90)	3.62 (1.49-8.83)	0.005
After first-line treatment with a SGA (n=2,311)	3.36 (2.30-4.90) <sup>b</sup>	4.08 (1.87-8.91) <sup>b</sup>	<0.001
	3.27 (2.40-4.45) <sup>c</sup>	3.67 (1.80-7.49) <sup>c</sup>	<0.001
<b>Risks with starting olanzapine</b>			
Before starting olanzapine (n=7,652) <sup>d</sup>	3.41 (2.78-4.17)	1.00 (Reference)	-
After starting olanzapine (n=2,115)	4.79 (3.72-6.17)	1.94 (1.39-2.71)	<0.001
<b>Risks with starting aripiprazole</b>			
Before starting aripiprazole (n=8,358) <sup>e</sup>	3.39 (2.83-4.07)	1.00 (Reference)	-
After starting aripiprazole (n=2,719)	4.93 (3.79-6.42)	2.19 (1.57-3.07)	<0.001
<b>Risks with starting clozapine</b>			



Before starting clozapine (n=9,159) <sup>f</sup>	3.58 (3.05-4.19)	1.00 (Reference)	-
After starting clozapine (n=862)	7.19 (5.09-10.17)	3.25 (2.19-4.82)	<0.001

IR= Incidence rates of type 2 diabetes mellitus (T2DM) per 1000 person-years; AHR= Adjusted Hazard Ratios that were estimated by cox proportional hazard regression models. These models included gender, family history of DM, and urbanicity as time-independent covariates, and calendar period, Defined Daily Doses (DDD) of antipsychotics, DDD of valproate, and DDD of tricyclic or tetracyclic antidepressants as time-dependent covariates. FGA= First Generation Antipsychotic drugs; SGA= Second Generation Antipsychotic drugs; <sup>a</sup> People with schizophrenia, who were antipsychotic naïve at the time of diagnosis of schizophrenia; <sup>b</sup> All SGA except Olanzapine and Clozapine; <sup>c</sup> All SGA except Clozapine; <sup>d</sup> People with schizophrenia, who had received olanzapine before their diagnosis of schizophrenia, were excluded from this analysis; <sup>e</sup> People with schizophrenia, who had received aripiprazole before their diagnosis of schizophrenia, were excluded from this analysis; <sup>f</sup> People with schizophrenia, who had received clozapine before their diagnosis of schizophrenia, were excluded from this analysis.

**eFigure 1:** Flow chart presenting identification of people with Diabetes Mellitus (DM) on the basis of hospital contacts and prescriptions, filled for antidiabetic drugs



\*Overlap: 53 filled a prescription for an antidiabetic drug on the day of a general hospital contacts; T1DM: type 1 Diabetes Mellitus; ICD-10: E10; O24.0; ICD-8: 249; T2DM: Type 2 Diabetes Mellitus; ICD-10: E11; O24.1; ICD-8: 250; Other: ICD 10: E12-14, H36.0, O24.2, O24.3, O24.5, O24.9;

Among the 14,118 new-onset DM, 4,277 could be identified as T2DM at the time of their first DM diagnoses. In the sensitivity analysis we identified 5,488 as T2DM when disregarding earlier contacts with T1DM codes.

