Supplemental data

Appendix S1: Antipsychotic drugs and their Anatomical Therapeutic Chemical (ATC) classification system codes

ATC code	Antipsychotic drug
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
N05AG02	Pimozide

ATC code	Antipsychotic drug
N05AG03	Penfluridol
N05AD03	Melperone
N05AE03	Sertindole
N05AE04	Ziprasidone
N05AH02	Clozapine
N05AH03	Olanzapine
N05AH04	Quetiapine
N05AH05	Asenapine
N05AL01	Sulpiride
N05AL05	Amisulpride
N05AX08	Risperidone
N05AX12	Aripiprazole
N05AX13	Paliperidone

Appendix S2: Age-specific incidence rates of type-2 diabetes mellitus in people with and without schizophrenia

Age group (years)	People without schizophrenia				People with schizophrenia			
	Person-years (millions)	Incident diabetes (n)	Incidence rates [a]	95% CI	Person-years	Incident diabetes (n)	Incidence rates [a]	95% CI
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
0-36	**49.61**	**5,302**	**0.11**	**0.10-0.11**	**47,519.08**	**186**	**3.91**	**3.39-4.52**

[a] Incidence rates of type-2 diabetes mellitus per 1000 person-years

Appendix S3: Endogenous risk for type-2 diabetes mellitus in antipsychotic naive people with schizophrenia

	Incidence rates [a]	**95% CI** [a]	**Adjusted hazard-ratio**	**95% CI**	**p-value**
Follow-up censored at first antipsychotic prescription [b]					
People without schizophrenia (N=2,736,510) [c]	0.10	0.10-0.10	1.00	Reference	-
People with schizophrenia (n=4,322)	1.68	0.93-3.03	4.58 [d]	2.53-8.28 [d]	<0.001
People with schizophrenia (n=4,322)	1.68	0.93-3.03	4.71 [e]	2.60-8.51 [e]	<0.001
No use of antipsychotics during the entire follow-up [f]					
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[d]	1.75-8.71[d]	0.001
People with schizophrenia (n=1,154)	1.63	0.73-3.62	3.64 [e]	1.63-8.12 [e]	0.002

[a] Incidence rates of type-2 diabetes mellitus per 1000 person-years; [b] Data were censored at the earliest date among the following, date of diagnosis of potential type-2 diabetes diagnoses, date of starting any antipsychotic medication, date of death, date of emigration from Denmark,

and the end of follow-up on 01/01/2013; [c] Assuming that the people with schizophrenia were at risk for DM after the diagnosis of schizophrenia, analyses were carried out with reference groups including data of people without schizophrenia, and of antipsychotic naive people with schizophrenia before the diagnosis of schizophrenia; [d] adjusted for the effects of gender, family history of diabetes, and urbanicity; [e] Adjusted for the effects of gender, family history of diabetes, urbanicity, exposure to valproate, and exposure to tricyclic or tetracyclic antidepressants; [f] Endogenous risk for diabetes in people with schizophrenia, who remained antipsychotic naive until the end of follow-up, was evaluated with reference to people without schizophrenia, who have not been exposed to any antipsychotic medications.

Appendix S4: Risperidone, Quetiapine, and Ziprasidone related risks for diabetes mellitus in people with schizophrenia

	Incidence rates [a]	**95% CI [a]**	**Adjusted hazard-ratio [b]**	**95% CI [b]**	**p-value**
Risks with starting risperidone					
Before starting risperidone (n=7,600) [c]	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
Risks with starting quetiapine					
Before starting quetiapine (n=7,745) [d]	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
Risks with starting ziprasidone					
Before starting ziprasidone (n=8,817) [e]	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

[a] Incidence rates of diabetes mellitus per 1000 person-years; [b] Adjusted hazard-ratios that were estimated by cox proportional hazard regression models. These models included gender, family history of diabetes, 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; [c] People with schizophrenia, who had received risperidone before their diagnosis of schizophrenia, were excluded from this analysis: [d] People

with schizophrenia, who had received quetiapine before their diagnosis of schizophrenia, were excluded from this analysis; [e] People with schizophrenia, who had received ziprasidone before their diagnosis of schizophrenia, were excluded from this analysis.

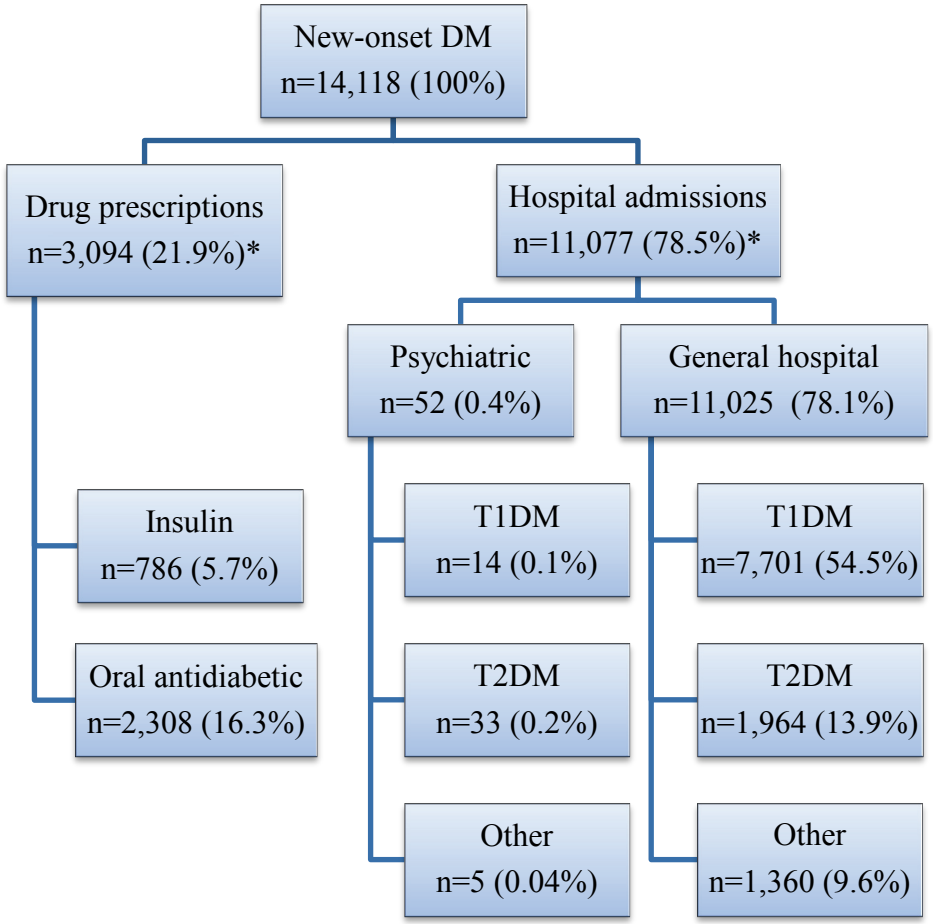
Appendix S5: Antipsychotic-related risks for Type-2 Diabetes Mellitus in people with schizophrenia

Risks with starting antipsychotics	**Incidence rates** [a]	**95% CI** [a]	**Adjusted hazard-ratio** [b]	**95% CI** [b]	**p-value**
Before starting any antipsychotic medication (n=4,322) [c]	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 first-generation antipsychotic medication (n=450)	3.92	2.23-6.90	3.62	1.49-8.83	0.005
After first-line treatment with a second-generation antipsychotic medication (n=1,708) [d]	3.36	2.30-4.90	4.08	1.87-8.91	<0.001
After first-line treatment with a second-generation antipsychotic medication (n=2,311) [e]	3.27	2.40-4.45	3.67	1.80-7.49	<0.001
Risks with starting olanzapine					
Before starting olanzapine (n=7,652) [f]	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
Risks with starting aripiprazole					
Before starting aripiprazole (n=8,358) [g]	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
Risks with starting clozapine					
Before starting clozapine (n=8,890) [h]	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

[a] Incidence rates of potential type-2 diabetes mellitus per 1000 person-years; [b] Adjusted hazard-ratios that were estimated by cox proportional hazard regression models. These models included gender, family history of diabetes, 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; [c] People with schizophrenia, who were antipsychotic naive at the time of diagnosis of schizophrenia; [d] Starting monotherapy with all second-generation antipsychotics except Olanzapine and Clozapine; [e] Starting monotherapy with all second-generation antipsychotics except Clozapine; [f] People with schizophrenia, who had received olanzapine before their diagnosis of schizophrenia, were excluded from this analysis: [g] People with schizophrenia, who had received aripiprazole before their diagnosis of schizophrenia, were excluded from this analysis; [h] People with schizophrenia, who had received clozapine before their diagnosis of schizophrenia, were excluded from this analysis.

Figure S1: Flow chart presenting identification of people with Diabetes Mellitus (DM) on the basis of hospital admissions, prescriptions, and filled for antidiabetic drugs



*Overlap: 53 filled a prescription for an antidiabetic drug on the day of a general hospital admission; 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 8/10: E12-14, H36.0, O24.2, O24.3, O24.5, O24.9; Among the 14,118 new-onset DM, 4,277 could be recognised as T2DM at the time of their first DM diagnoses.

Figure S2: Age-specific incidence rates of diabetes mellitus in people with and without schizophrenia