Data supplement for Solmi et al., Effectiveness of Antipsychotic Use for Reducing Risk of Work Disability: Results From a Within-Subject Analysis of a Swedish National Cohort of 21,551 Patients With First-Episode Nonaffective Psychosis. Am J Psychiatry (doi: 10.1176/appi.ajp.21121189)

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Methods

PRE2DUP method

Among several methods developed and used to measure drug use periods, PRE2DUP is a validated and accurate method that goes beyond simplistic and fixed assumptions[16,40,41]. PRE2DUP accounts for each individual's purchase history, building exposure time periods and estimating the drug dose based on the purchased Defined Daily Doses. PRE2DUP accounts for stockpiling of drugs, pattern of purchasing (i.e., regularity), as well as inpatient hospital periods when drug use is not recorded in the Prescribed Drug Register. Modelling of drug use periods is controlled via expert-defined parameters designed for each drug package (identified through Nordic Article number, vnr) and thus, for each package size, drug formulation and strength. The method also enables separate modelling of oral versus long-acting injectable antipsychotics which have different use patterns. The method is particularly valid for long-term medications, such as antipsychotics.

TABLE S1. Events, person-years (PY) (with event) by antipsychotic treatment.

	Events	PY	PY with event
No treatment	9,930	47,545	20,489
Olanzapine	1,519	6,216	3,276
AP Polytherapy	1,237	3,407	1,808
Aripiprazole	792	2,859	1,693
Quetiapine	787	2,660	1,552
Risperidone	748	2,769	1,610
Other oral AP	718	2,292	1,354
Any LAI	344	1,335	669

AP, antipsychotic; LAI, long-acting injectable antipsychotic

TABLE S2. Users, events and person-years (PYs) of monotherapies of specific long-acting injectables (LAIs) and their corresponding oral formulations (OAP). Adjusted Hazard Ratios (aHRs) for sickness absence or disability pension presented in comparison with non-use of all antipsychotics. Of LAI users, n=5 users of fluphenazine LAI were omitted as HR could not be calculated due to lack of events and no one used fluphenazine OAP in monotherapy. Adjusted for use of other antipyschotics, antidepressants, mood stabilizers, benzodiazepines and related drugs, temporal order of treatments and time since cohort entry.

	OAP			**LAI**			**OAP**	**LAI**
Drug	Users	Events	PYs	Users	Events	PYs	aHR (95%CI)	aHR (95%CI)
Risperidone	3323	748	2769	349	93	316	0.72 (0.58-0.88)	0.40 (0.24-0.67)
Paliperidone	326	93	265	280	64	214	0.65 (0.40-1.04)	0.27 (0.12-0.63)
Perphenazine	418	106	376	234	55	200	0.90 (0.61-1.35)	0.60 (0.31-1.15)
Zuclopenhixol	349	76	205	257	51	193	0.73 (0.44-1.22)	0.58 (0.26-1.32)
Haloperidol	849	166	521	148	27	136	0.81 (0.55-1.18)	0.29 (0.09-0.96)
Olanzapine	7531	1519	6216	187	23	126	0.68 (0.59-0.78)	1.11 (0.33-3.81)
Aripiprazole	3349	792	2859	172	21	100	0.68 (0.56-0.82)	0.62 (0.25-1.54)
Flupentixol	363	122	378	48	9	32	0.64 (0.39-1.04)	0.29 (0.06-1.57)
Any LAI vs. corresponding OAP	12212	3622	13589	1436	343	1317	reference[1]	0.66 (0.49-0.90)

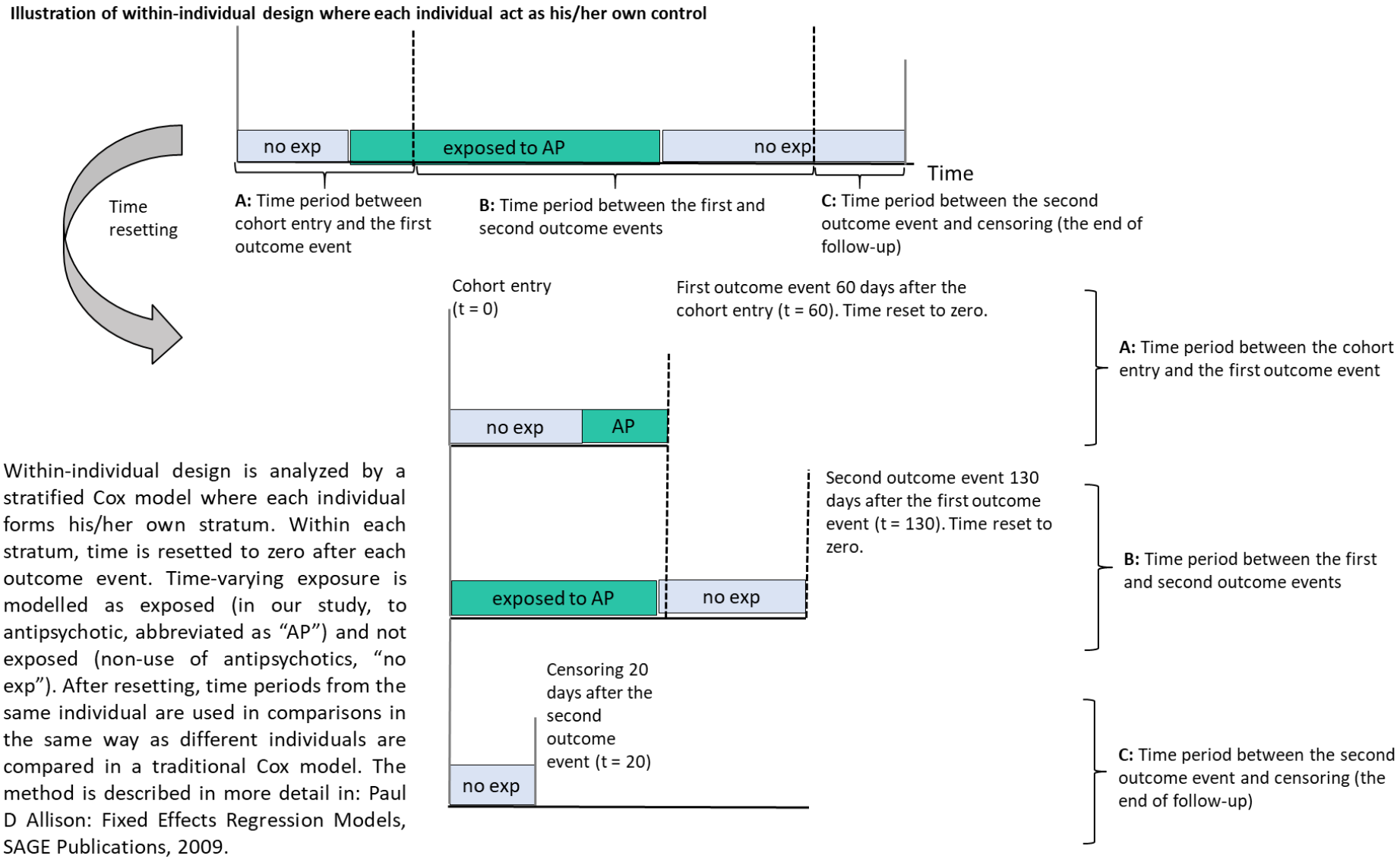
[1]In this comparison, any LAI is compared with corresponding OAPs as a reference.

TABLE S3. Risk of sickness absence or disability pension during antipsychotic (AP) use versus non-use in patients with first-episode non-affective psychosis, within-individual analyses, within two years, between two to five years, and more than five years since non-affective psychosis onset.

	<2 years	**2-5 years**	**>5 years**
Any AP vs no	0.64 (0.50-0.82)	0.63 (0.50-0.79)	0.59 (0.46-0.75)
Any LAI	0.20 (0.08-0.49)	0.43 (0.21-0.91)	0.34 (0.18-0.63)
AP polytherapy	0.51 (0.31-0.82)	0.59 (0.36-0.96)	0.51 (0.29-0.90)
Risperidone	0.60 (0.35-1.00)	0.99 (0.59-1.67)	0.62 (0.30-1.25)
Other oral AP	0.64 (0.40-1.01)	0.60 (0.38-0.94)	0.65 (0.40-1.06)
Olanzapine	0.70 (0.50-0.97)	0.57 (0.39-0.83)	0.52 (0.34-0.80)
Quetiapine	0.74 (0.43-1.27)	0.63 (0.40-0.99)	0.82 (0.51-1.32)
Aripiprazole	0.78 (0.47-1.31)	0.63 (0.41-0.96)	0.58 (0.37-0.91)

AP, antipsychotic; LAI, long-acting injectable antipsychotic

FIGURE S1. Study design



Within-individual design is analyzed by a stratified Cox model where each individual forms his/her own stratum. Within each stratum, time is resetted to zero after each outcome event. Time-varying exposure is modelled as exposed (in our study, to antipsychotic, abbreviated as "AP") and not exposed (non-use of antipsychotics, "no exp"). After resetting, time periods from the same individual are used in comparisons in the same way as different individuals are compared in a traditional Cox model. The method is described in more detail in: Paul D Allison: Fixed Effects Regression Models, SAGE Publications, 2009.

FIGURE S2. Development of main occupational activity of persons with first-episode non-affective psychosis, from 2 calendar years before and until 5 years after the first diagnoses, stratified by A) antipsychotic use (N=14,392) vs. B) non-use (N=7,159) during the follow-up. Timepoint 0 refers to the year of first psychosis diagnosis.

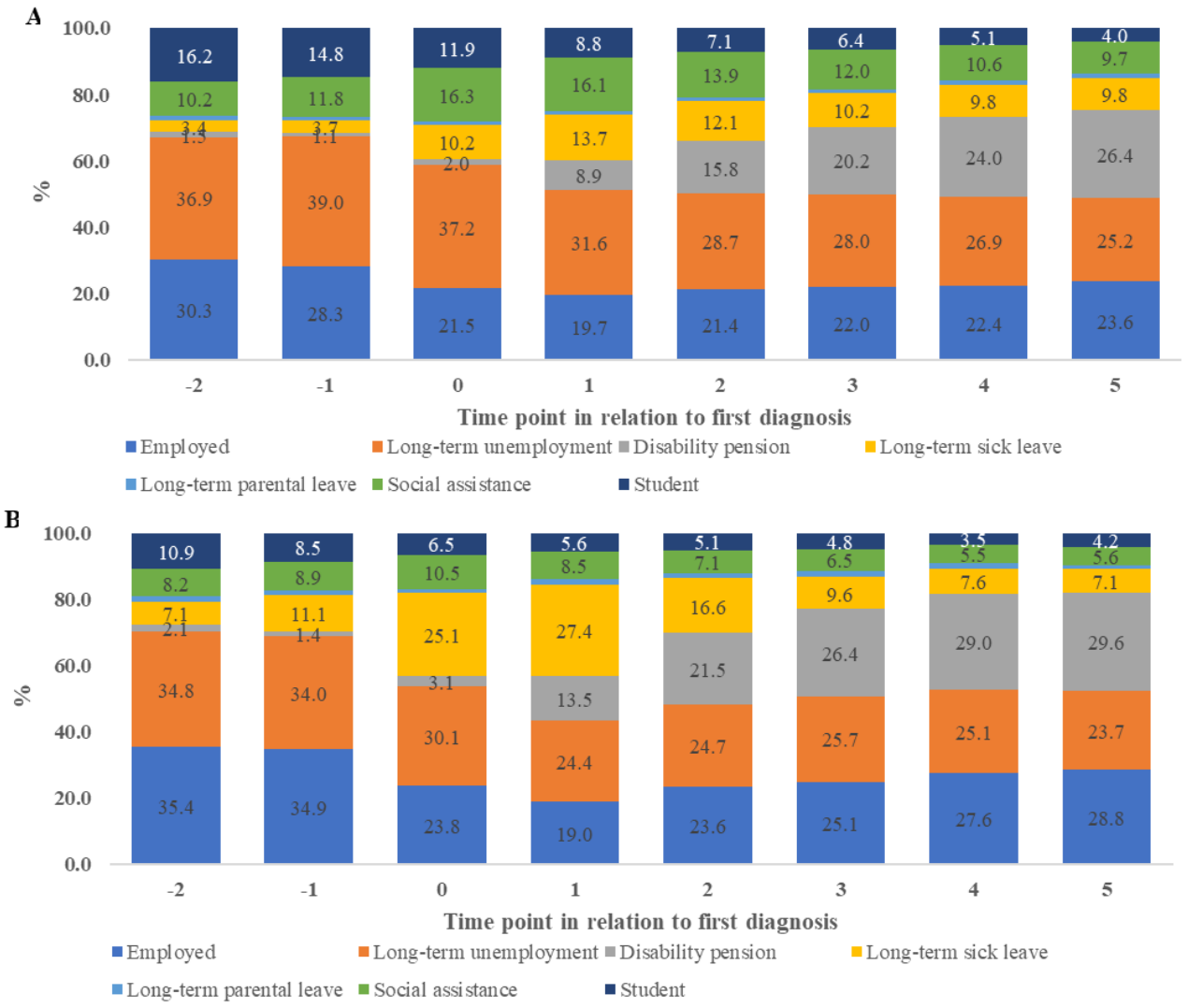


FIGURE S3. Development of main occupational activity of persons with first-episode non-affective psychosis, from 2 calendar years before and until 5 years after the first diagnoses among those diagnosed during 2006-2011 who had five years of follow-up time in terms of data linkage (up until end of 2016), stratified by A) antipsychotic use (N=7,849) vs. B) non-use (N=3,186) during the follow-up. Timepoint 0 refers to the year of first psychosis diagnosis.

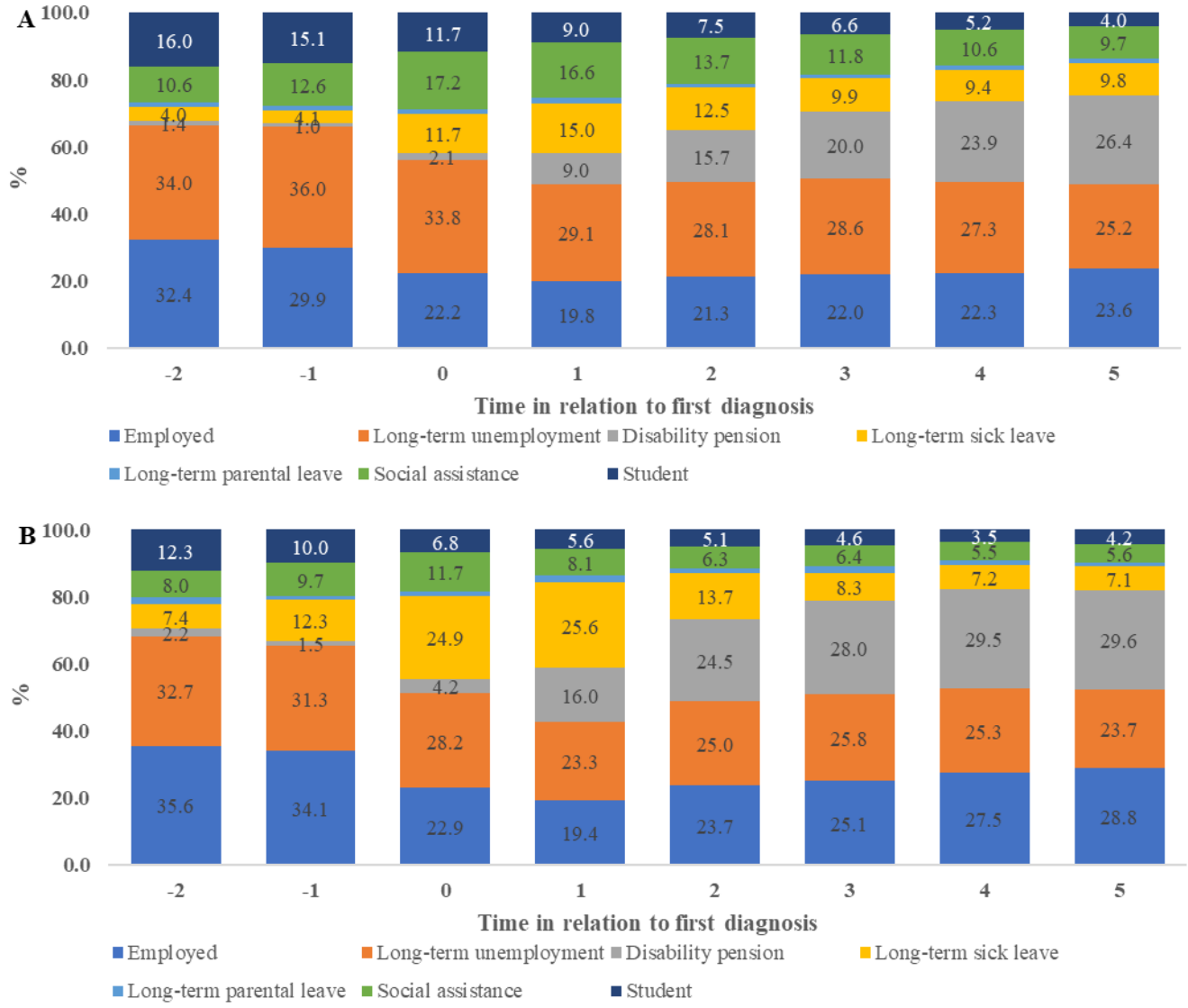
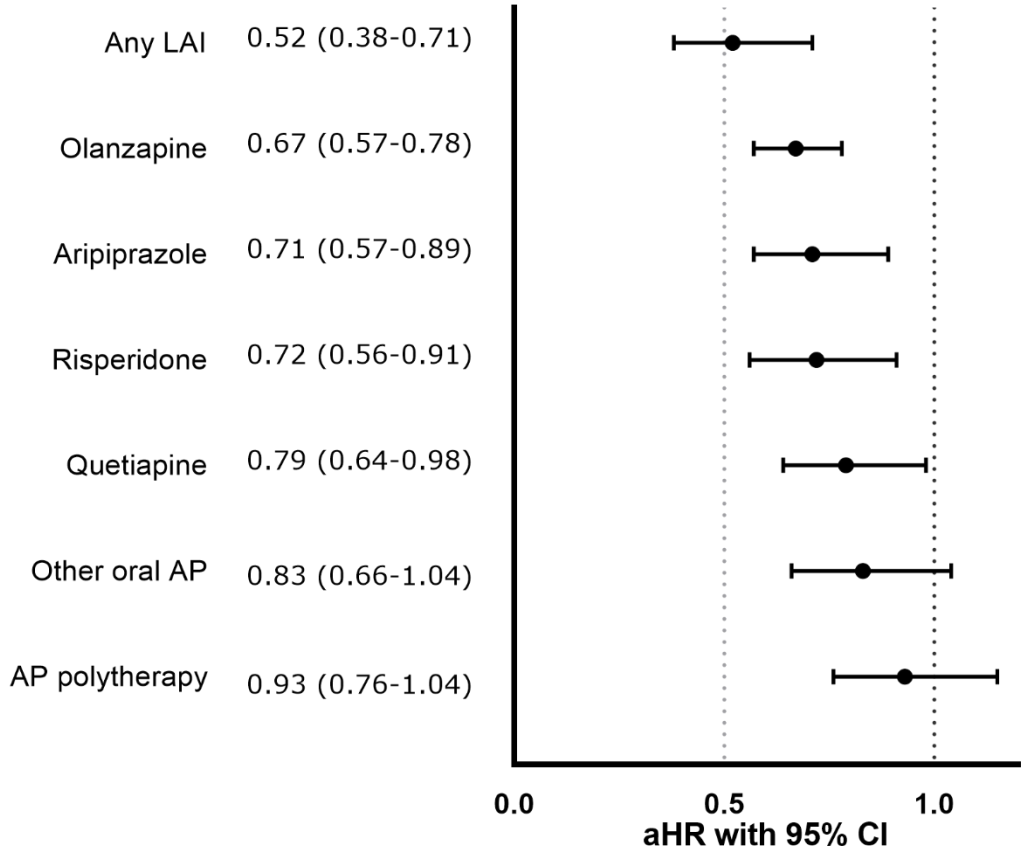
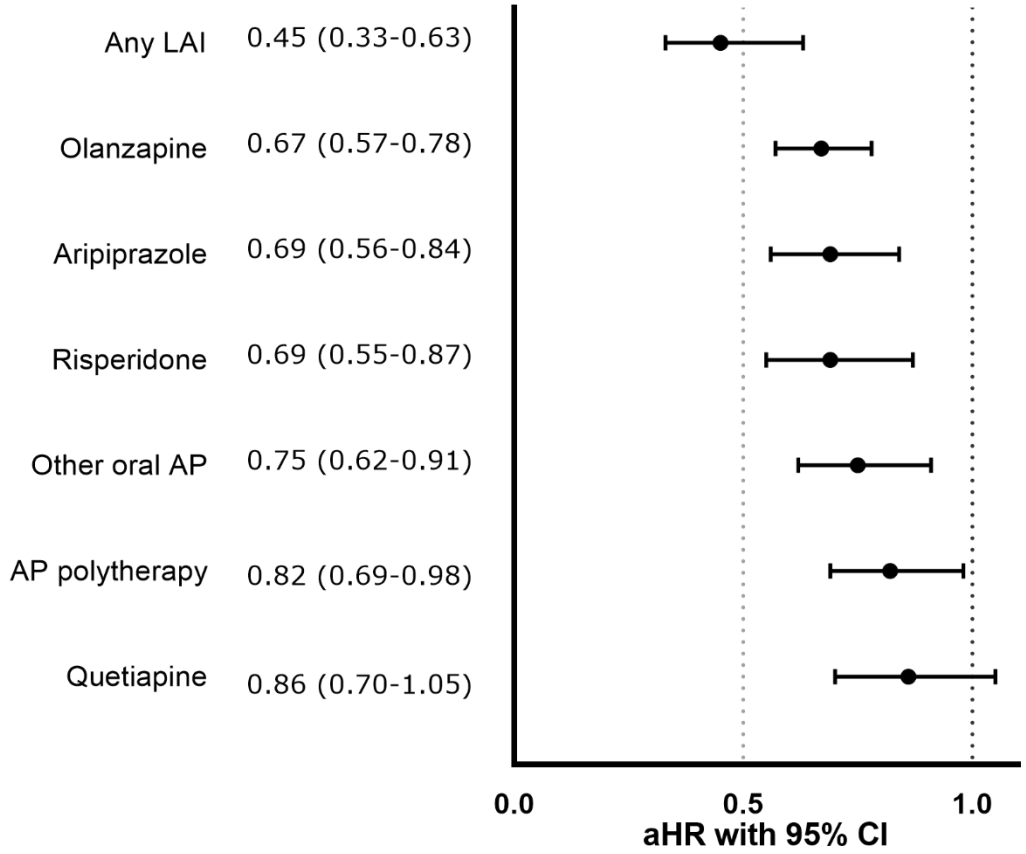


FIGURE S4. Risk of sickness absence or disability pension antipsychotic during use versus non-use in patients with first-episode non-affective psychosis, within-individual sensitivity analysis in those without antipsychotic use during one year before diagnosis.



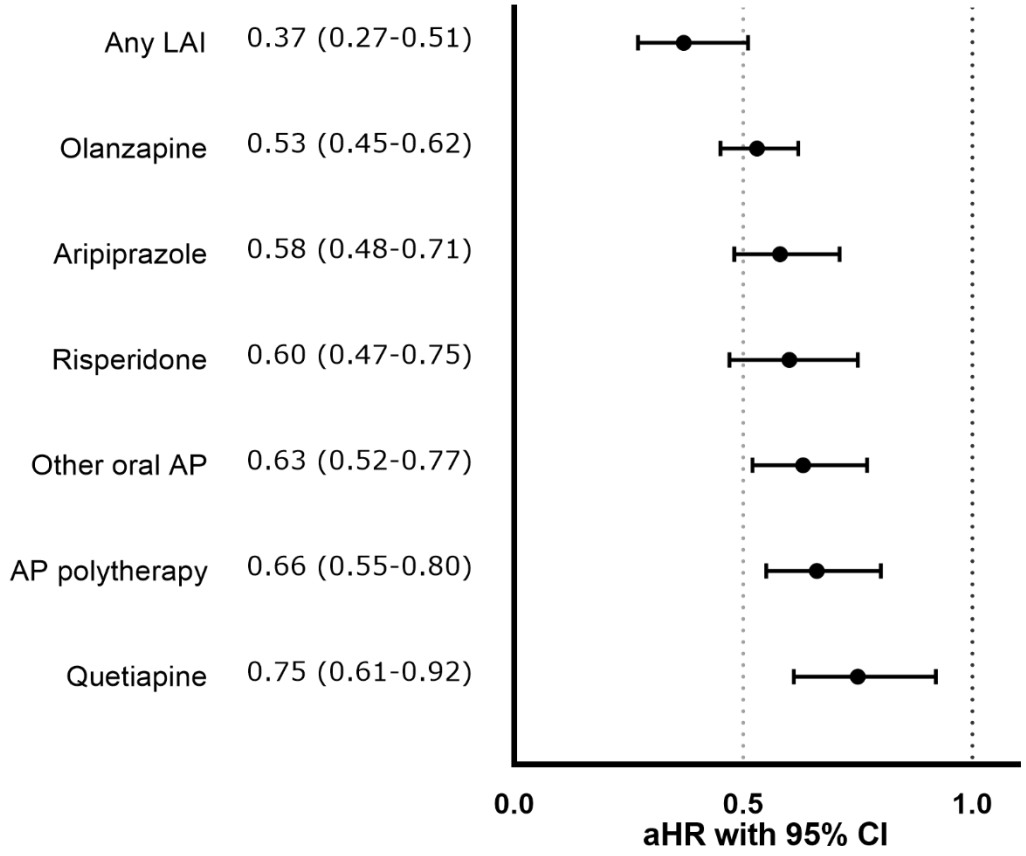
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S5. Risk of sickness absence or disability pension antipsychotic during use versus non-use in patients with first-episode non-affective psychosis, within-individual sensitivity analysis in those without sickness absence at baseline.



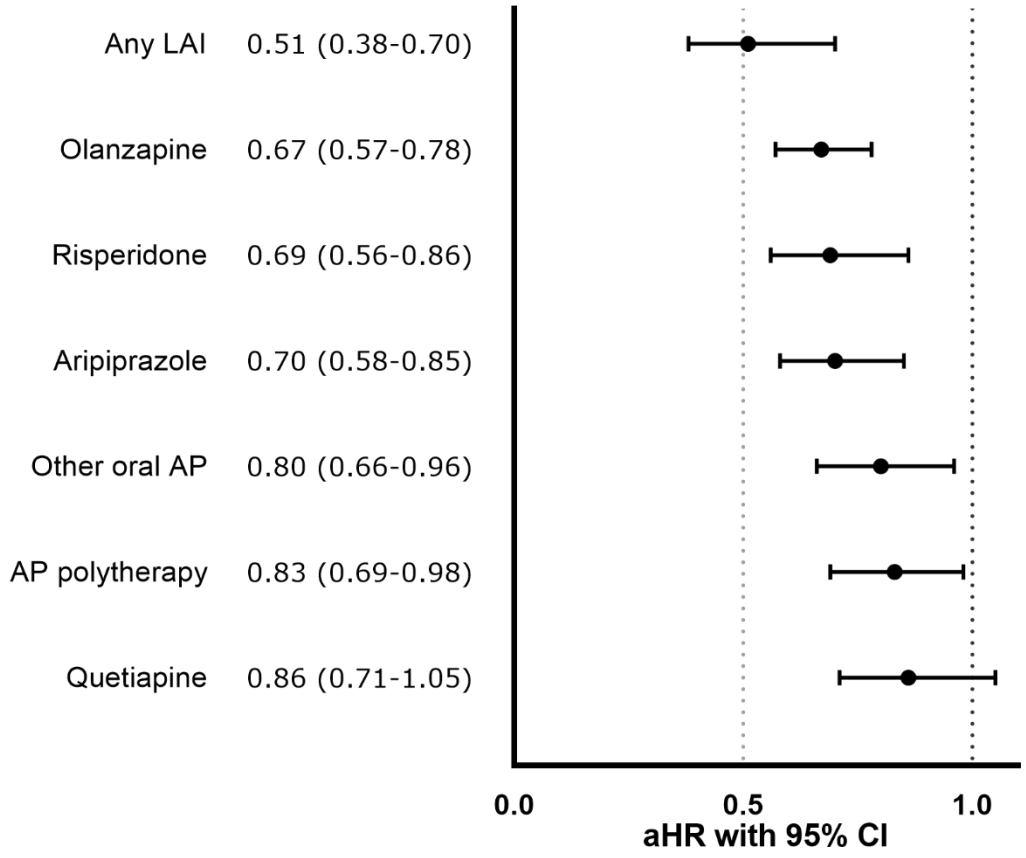
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S6. Risk of sickness absence or disability pension antipsychotic during use versus non-use in patients with first-episode non-affective psychosis, within-individual sensitivity analysis when the first 30 days was censored from all exposures.



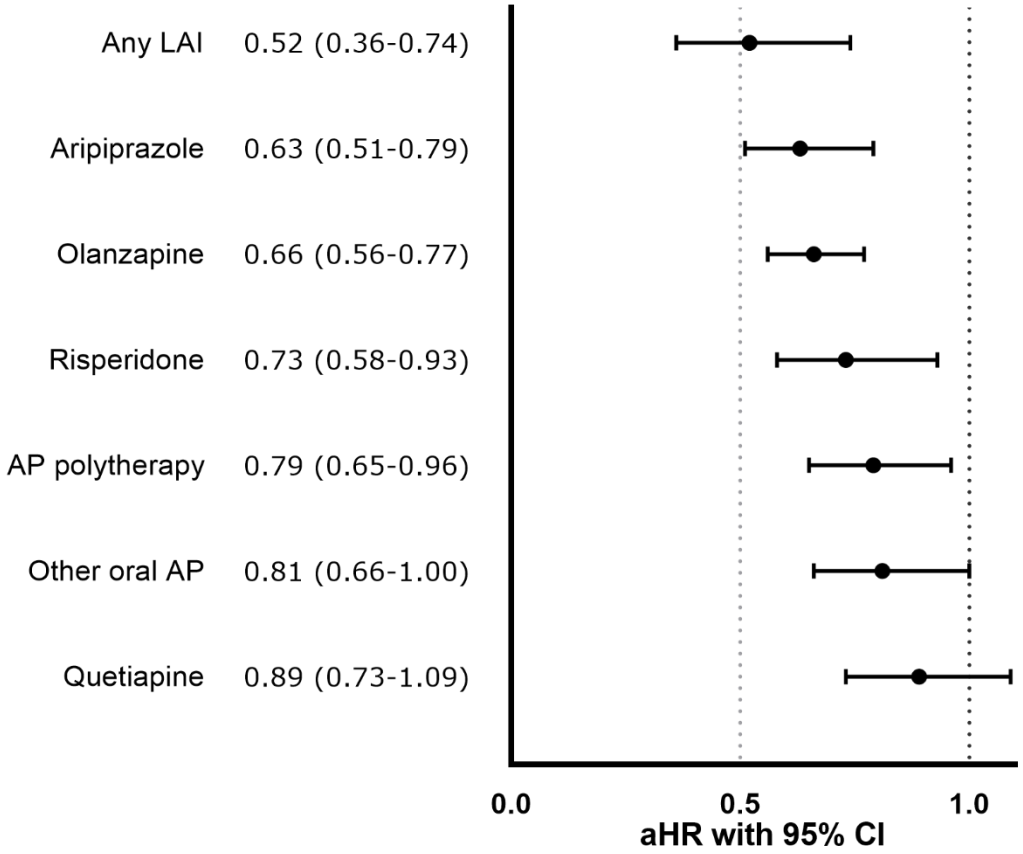
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S7. Risk of sickness absence during antipsychotic use versus non-use in patients with first-episode non-affective psychosis, within-individual sensitivity analysis (censoring to disability pension).



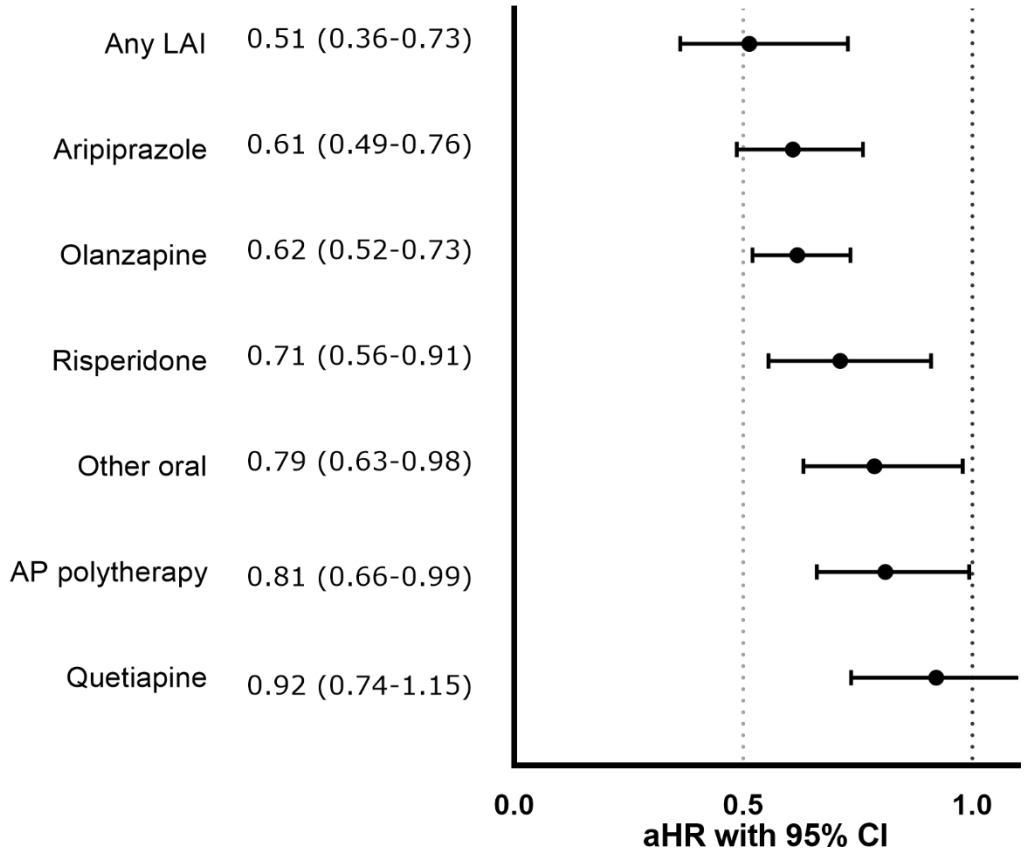
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S8. Risk of sickness absence during antipsychotic use versus non-use in patients with first-episode non-affective psychosis, within-individual sensitivity analysis among those who were not granted with disability pension ever during the follow-up.



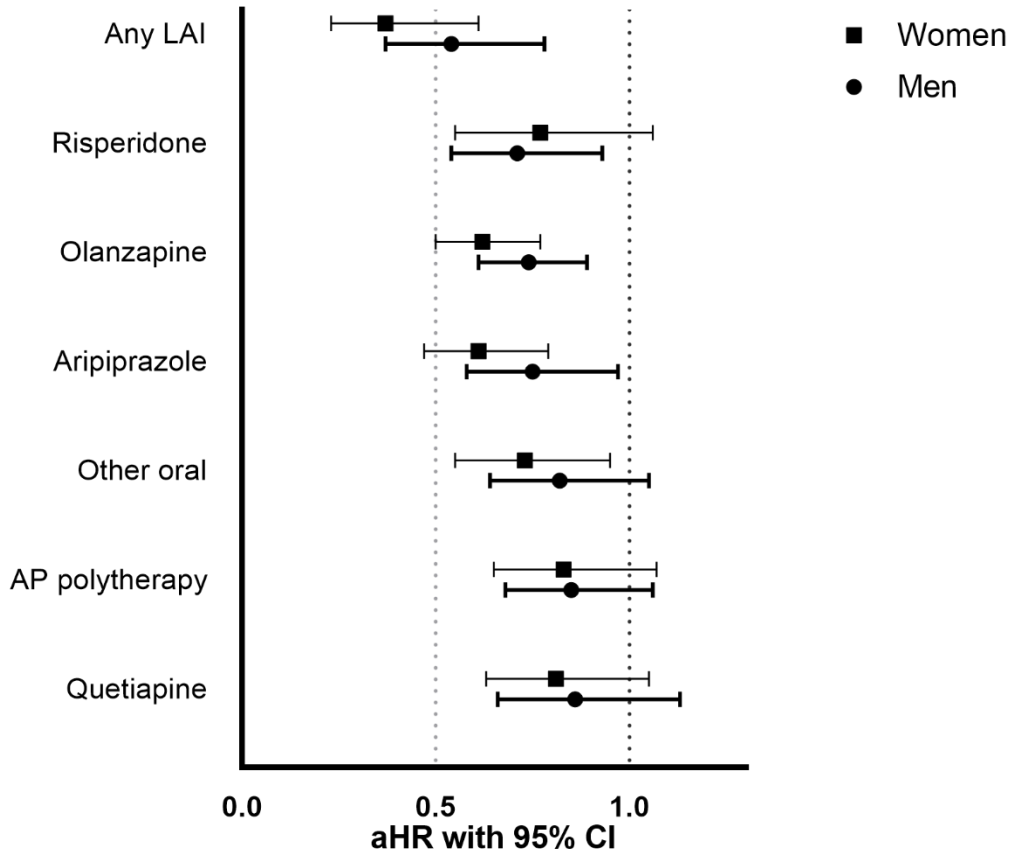
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S9. Risk of sickness absence or disability pension during antipsychotic use versus non-use in patients with first-episode non-affective psychosis, within-individual analyses among those who were employed during previous year before cohort entry.



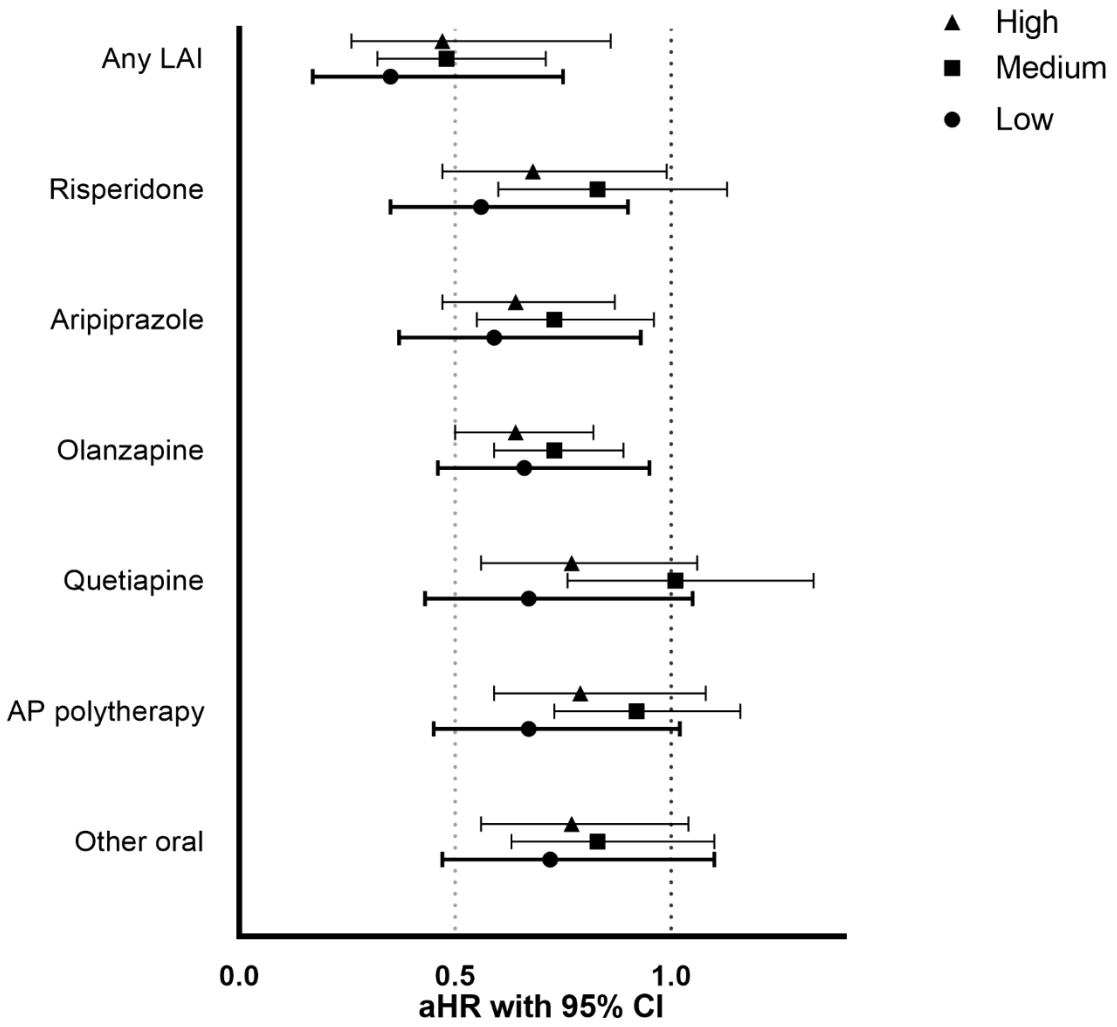
AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S10. Risk of sickness absence or disability pension during antipsychotic use versus non-use in patients with first-episode non-affective psychosis, within-individual analyses stratified by gender.



AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic

FIGURE S11. Risk of sickness absence or disability pension during antipsychotic use versus non-use in patients with first-episode non-affective psychosis, within-individual analyses stratified by baseline educational level.



AP, antipsychotic; CI, confidence interval; aHR, adjusted Hazard ratio; LAI, long-acting injectable antipsychotic