

Supplementary material to

Real-world effectiveness of antidepressants, antipsychotics and their combinations in the maintenance treatment of psychotic depression. Evidence from within-subject analyses of two nationwide cohorts

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Heidi Taipale, Johannes Lieslehto, Markku Lähteenvuo, Aleksi Hamina, Antti Tanskanen, Ellenor Mittendorfer-Rutz, Tapio Paljärvi, Marco Solmi, Andrea Cipriani, Christoph U. Correll, Jari Tiihonen

Supplementary Figure 1A. Description of study design, exposure periods and time resetting in the within-individual design.

Supplementary Figure 1B. Detailed description of exposure coding.

Supplementary Figure 2. Correlation of the effectiveness of antidepressant (AD) results (i.e., adjusted Hazard Ratios) in preventing psychiatric hospitalization in patients with psychotic depression between the Finnish and Swedish cohorts.

Supplementary Figure 3. Correlation of effectiveness of the antipsychotic results (i.e., adjusted Hazard Ratios) in preventing psychiatric hospitalization in patients with psychotic depression between the Finnish and Swedish cohorts.

Supplementary Table 1. Characteristics of Finnish and Swedish cohorts.

Supplementary Table 2. Risk of psychiatric hospitalization associated with specific antipsychotics (AP) and specific antidepressants (AD) when the first 30 days were removed from all use periods, in within-individual models of the Finnish and Swedish cohorts, and in meta-analysis (MA).

Supplementary Table 3. Risk of psychiatric hospitalization associated with specific antipsychotics (AP) and specific antidepressants (AD), in between-individual models of the Finnish and Swedish cohorts, and in meta-analysis (MA).

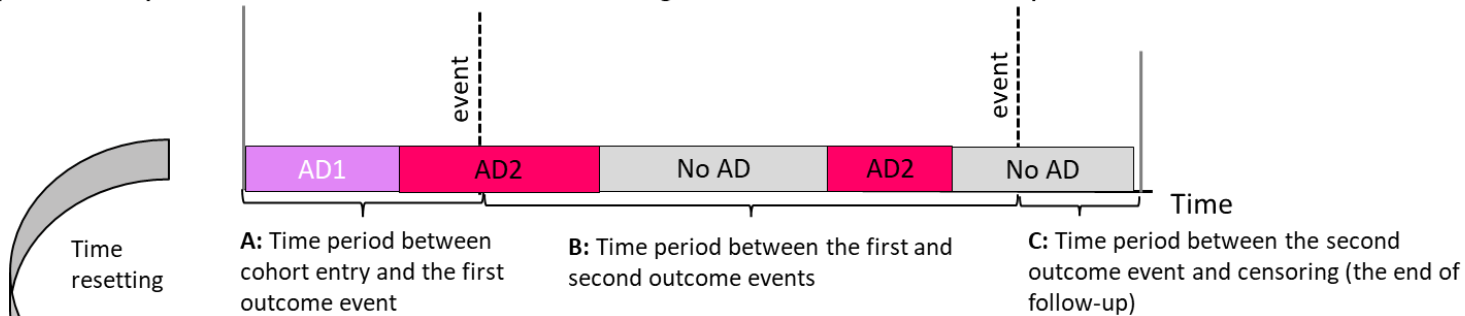
Supplementary Table 4. Risk of psychiatric hospitalization associated with specific antidepressants compared with non-use of antidepressants and specific antipsychotics compared with non-use of antipsychotics in fixed effects versus random effects meta-analysis (MA) based on within-individual Cox models of the Finnish and Swedish cohorts.

Supplementary Table 5. Risk of psychiatric hospitalization associated with specific antidepressants compared with non-use of antidepressants and specific antipsychotics compared with non-use of antipsychotics among those who do not experience diagnostic conversion to bipolar disorder or schizophrenia during the follow-up, in fixed effects meta-analysis (MA) based on within-individual Cox models of the Finnish and Swedish cohorts.

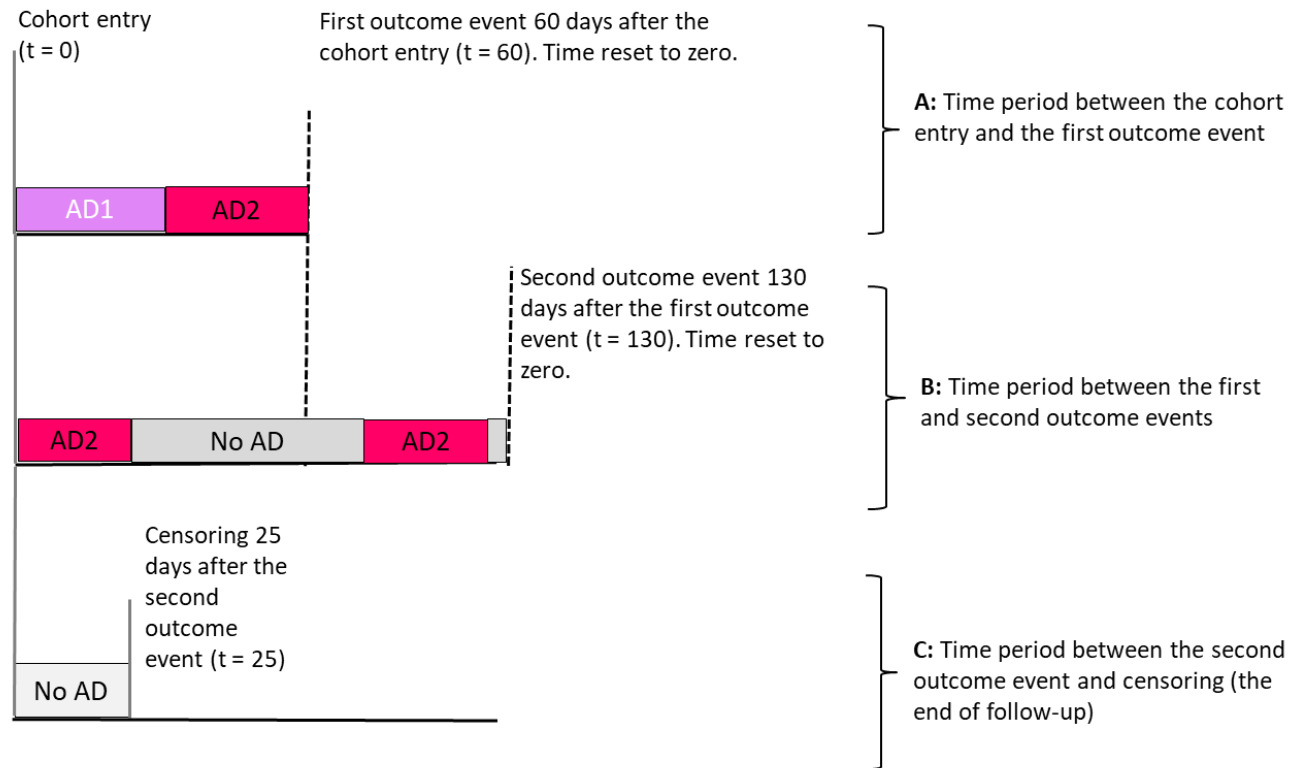
Supplementary Table 6. Risk of psychiatric hospitalization associated with two-drug combinations of most common antipsychotics and antidepressants and use of antidepressant only or antipsychotic only, with reference to non-use of both antipsychotics and antidepressants in within-individual design, in the Finnish and Swedish cohorts.

Supplementary Figure 1A. Description of study design, exposure periods and time resetting in the within-individual design.

Principles how comparisons are conducted in within-individual design where each individual act as his/her own control

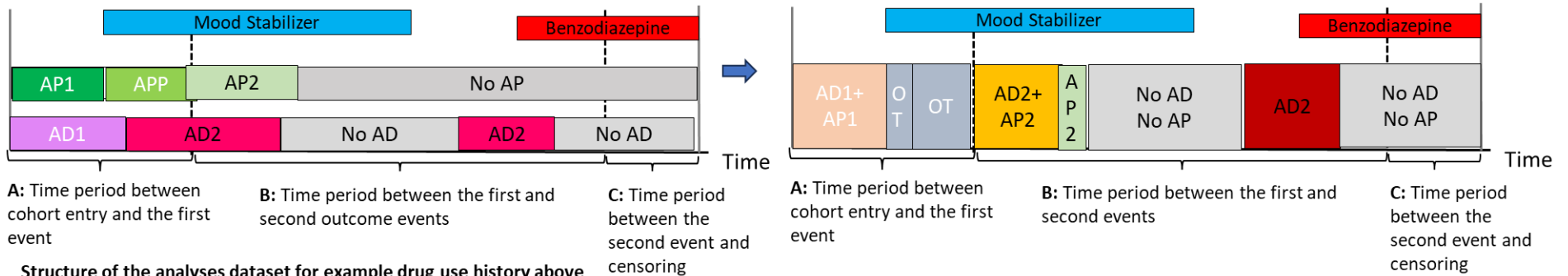


Each individual forms his/her own stratum. Within each stratum, time is reset after each outcome event. Exposure is time-varying use (as different specific drugs, antidepressants AD in this example, AD1 and AD2) vs. non-use of the drug class (“No AD”). Within-individual design is analyzed as stratified Cox model. 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: Paul D Allison: Fixed Effects Regression Models, SAGE Publications, 2009.



Supplementary Figure 1B. Detailed description of exposure coding.

Comparisons when analyzing antidepressant (AD), antipsychotic (AP) and antidepressant-antipsychotic pairs.



Structure of the analyses dataset for example drug use history above

row#	ID	start	stop	AD	MS	AP	BE	series	censor	init	end
1	3	1	29	AD1	0	AP1	0	1	0	1	29
2	3	30	60	AD2	1	APP	0	1	1	30	60
3	3	61	92	AD2	1	AP2	0	2	0	1	32
4	3	93	98	NoAD	1	AP2	0	2	0	33	38
5	3	99	130	NoAD	1	NoAP	0	2	0	39	70
6	3	131	140	NoAD	0	NoAP	0	2	0	71	80
7	3	141	169	AD2	0	NoAP	0	2	0	81	109
8	3	169	180	AD2	0	NoAP	1	2	0	109	120
9	3	181	190	NoAD	0	NoAP	1	2	1	121	130
10	3	191	215	NoAD	0	NoAP	1	3	0	1	25

start and stop describe time since cohort entry (start=1) until the end of follow-up (stop=215) as days. These are the basis for between-individual model.

AP=antipsychotic describes time-varying use of two specific antipsychotics (AP1 and AP2), their concomitant use (APP) and non-use of antipsychotics (NoAP).

AD=antidepressant describes time-varying use of two specific antidepressants (AD1 and AD2) and non-use of antidepressants (No AD).

MS (mood stabilizer) and BE (benzodiazepine) describe time-varying use of these medications on drug-class level (1=use, 0=non-use).

series indicates which rows belong to the same series of within-individual model (when series changes time is reset to zero).

censor indicates whether the period ended at outcome event (censor=1) or censoring (censor=0). After censor=1, time is reset and the next row starts with init=1.

init and end assign time variable for within-individual model where time is reset to zero after each outcome event.

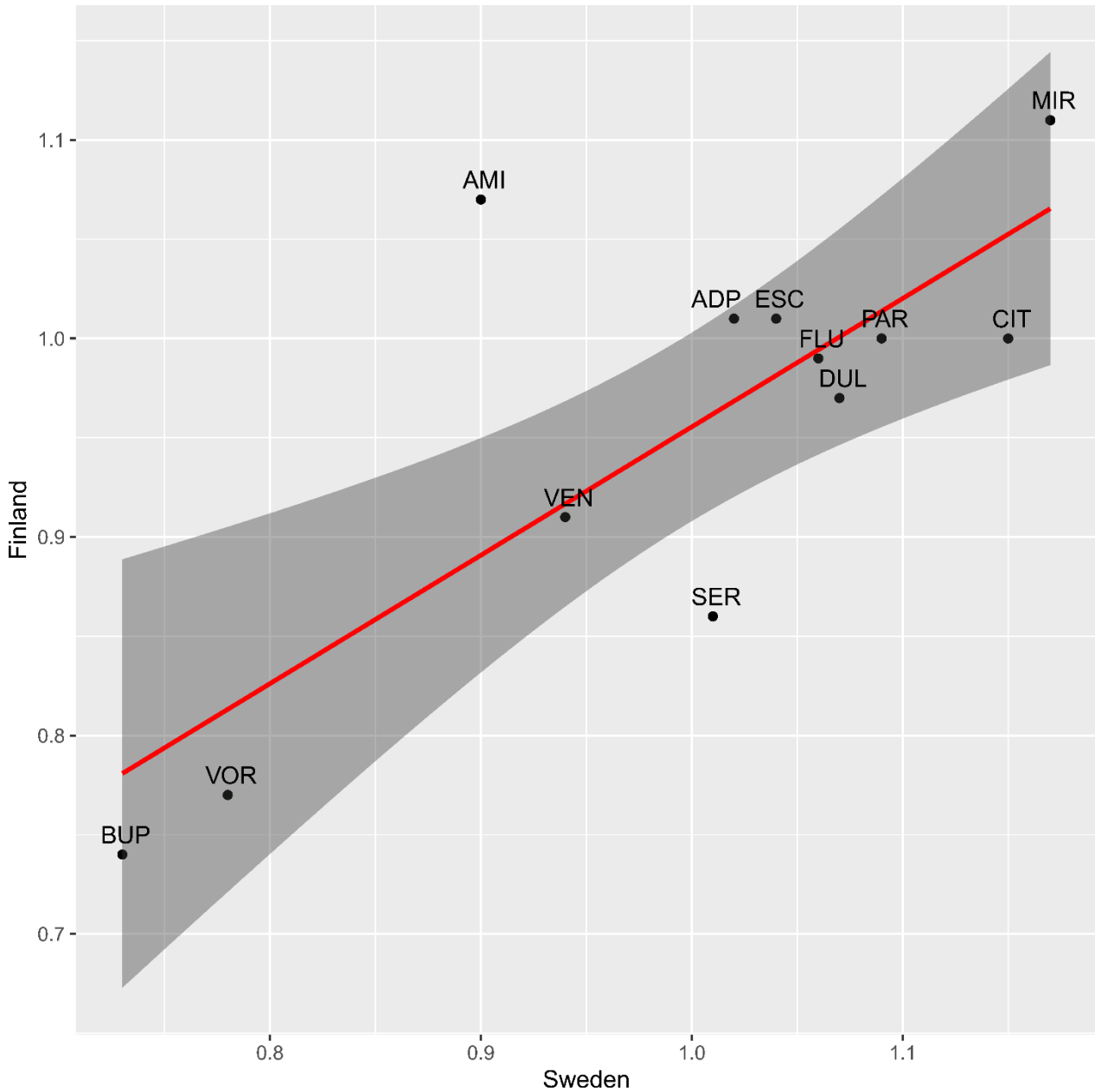
Row changes every time there is a change in exposures (AP, MS, AD or BE) or outcome event happens.

Antidepressant analyses compared use periods of AD1 and AD2 with "No AD" as reference, by adjusting for use of AP, MS and BE.

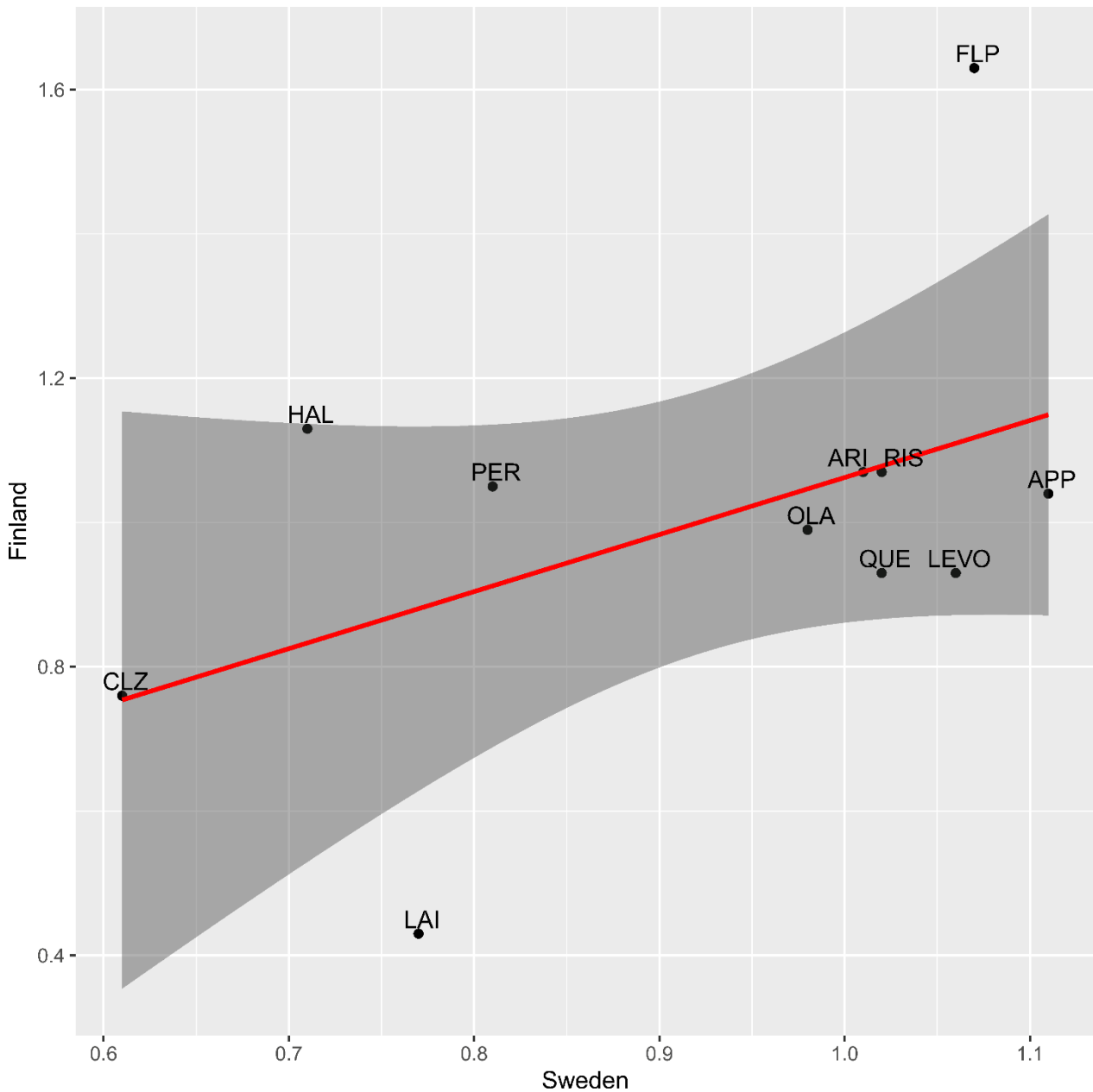
Antipsychotic analyses compared use periods of AP1, AP2 and APP with "No AP" Time periods as reference, by adjusting for use of AD, MS and BE.

Antidepressant-antipsychotic pair analyses (figure on right) compared use Of antidepressants and antipsychotics with non-use of both (No AD No AP), by adjusting for use of MS and BE. In these analyses, only two-drug pairs were specifically analyzed, in this example AD1+AP1, AD2+AP2, and "monotherapy" of one drug class only (in this example AP2 and AD2). OT refers to periods of more than 1 AD + 1 AP which were all grouped together and not reported.

Supplementary Figure 2. Correlation of the effectiveness of antidepressant (AD) results (i.e., adjusted Hazard Ratios) in preventing psychiatric hospitalization in patients with psychotic depression between the Finnish and Swedish cohorts. Pearson's $r=0.78$, $p=0.01$, $N=12$ antidepressants. The linear regression curve is depicted with a red line and the 95% confidence interval area for the curve is shown in dark grey. The x-axis shows adjusted hazard ratios in Sweden and the y-axis shows adjusted hazard ratios in Finland. AMI=amitriptyline, ADP=antidepressant polytherapy, BUP=bupropion, CIT=citalopram, DUL=duloxetine, ESC=escitalopram, FLU=fluoxetine, MIR=mirtazapine, PAR=paroxetine, SER=sertraline, VEN=venlafaxine, VOR=vortioxetine.



Supplementary Figure 3. Correlation of effectiveness of the antipsychotic results (i.e., adjusted Hazard Ratios) in preventing psychiatric hospitalization in patients with psychotic depression between the Finnish and Swedish cohorts. Pearson's $r=0.46$, $p=0.14$, $N=11$ antipsychotics. The linear regression curve is depicted with a red line and the 95% confidence interval area for the curve is shown in dark grey. The x-axis shows adjusted hazard ratios in Sweden and the y-axis shows adjusted hazard ratios in Finland. APP=antipsychotic polytherapy, ARI=aripiprazole oral, CLZ=clozapine, FLP=flupenthixol oral, HAL=haloperidol oral, LAI=any long-acting injectable antipsychotic, LEVO=levomepromazine, OLA=olanzapine oral, QUE=quetiapine, PER=perphenazine oral, RIS=risperidone oral.



Supplementary Table 1. Characteristics of Finnish and Swedish cohorts.

	Finnish cohort	Swedish cohort
	N=19330	N=13684
Mean age (SD)	39.8 (14.7)	41.3 (14.0)
Sex, % (N)		
Women	57.9 (11194)	53.5 (7325)
Men	42.1 (8136)	46.5 (6359)
Year of cohort entry, % (N)		
2000-2005	30.2 (5844)	NA
2006-2010	29.2 (5642)	31.7 (4336)
2011-2015	26.0 (5026)	33.3 (4559)
2016-*	14.6 (2818)	35.0 (4789)
Register source where patients were identified for the cohort		
Inpatient care register	36.6 (7277)	32.7 (4473)
Specialized outpatient register	47.8 (9237)	54.8 (4473)
Sick leave/ disability pension	14.6 (2816)	12.6 (1717)

*The Finnish cohort until 2018 and the Swedish cohort until 2021.

Supplementary Table 2. Risk of psychiatric hospitalization associated with specific antipsychotics (AP) and specific antidepressants (AD) when the first 30 days were removed from all use periods, in within-individual models of the Finnish and Swedish cohorts, and in meta-analysis (MA). Adjusted Hazard Ratios (aHRs) with 95% Confidence Intervals (CIs). LAI= long-acting injectable antipsychotic.

	Finnish cohort	Swedish cohort	Fixed effects MA
<i>Antipsychotics</i>	aHR (95%CI)	aHR (95%CI)	aHR (95%CI)
LAI	0.48 (0.29-0.77)	0.70 (0.44-1.10)	0.58 (0.42-0.81)
Clozapine	0.82 (0.60-1.11)	0.59 (0.35-0.99)	0.75 (0.58-0.98)
Haloperidol	1.30 (0.88-1.93)	0.78 (0.57-1.08)	0.96 (0.75-1.23)
Quetiapine	1.02 (0.95-1.09)	1.05 (0.95-1.16)	1.03 (0.97-1.09)
Levomepromazine	1.03 (0.88-1.20)	1.15 (0.95-1.40)	1.08 (0.95-1.22)
Aripiprazole	1.26 (1.07-1.47)	1.05 (0.90-1.23)	1.14 (1.02-1.28)
Olanzapine	1.21 (1.10-1.34)	1.12 (1.02-1.24)	1.17 (1.09-1.25)
Perphenazine	1.19 (1.00-1.42)	1.11 (0.65-1.90)	1.18 (1.00-1.40)
AP polytherapy	1.20 (1.11-1.30)	1.23 (1.12-1.36)	1.21 (1.14-1.29)
Risperidone	1.25 (1.12-1.38)	1.16 (0.99-1.35)	1.22 (1.12-1.33)
Flupentixol	1.35 (0.86-2.11)	1.18 (0.84-1.65)	1.24 (0.94-1.62)
<i>Antidepressants</i>			
Bupropion	0.73 (0.55-0.96)	0.72 (0.57-0.91)	0.72 (0.60-0.87)
Vortioxetine	0.96 (0.66-1.40)	0.80 (0.58-1.12)	0.87 (0.68-1.11)
Sertraline	1.00 (0.87-1.14)	1.09 (0.96-1.23)	1.05 (0.95-1.14)
Venlafaxine	1.07 (0.98-1.16)	1.08 (0.96-1.22)	1.07 (1.00-1.15)
Escitalopram	1.12 (1.00-1.26)	1.10 (0.96-1.26)	1.11 (1.02-1.21)
Citalopram	1.16 (1.03-1.31)	1.16 (0.93-1.45)	1.16 (1.04-1.29)
Duloxetine	1.12 (0.96-1.32)	1.19 (1.03-1.38)	1.16 (1.04-1.29)
AD polytherapy	1.22 (1.13-1.32)	1.08 (0.99-1.18)	1.16 (1.09-1.23)
Amitriptyline	1.31 (1.03-1.67)	1.03 (0.78-1.35)	1.18 (0.98-1.41)
Fluoxetine	1.14 (0.98-1.34)	1.24 (1.07-1.44)	1.19 (1.07-1.33)
Paroxetine	1.13 (0.93-1.37)	1.40 (1.07-1.83)	1.22 (1.04-1.42)
Mirtazapine	1.28 (1.16-1.42)	1.27 (1.12-1.43)	1.28 (1.18-1.38)
	1.23 (1.17-1.29)	1.26 (1.19-1.35)	1.24 (1.20-1.29)
Benzodiazepines and related drugs			
<i>Mood stabilizers</i>			
Carbamazepine	0.75 (0.53-1.06)	0.93 (0.70-1.24)	0.85 (0.69-1.06)
Lithium	0.86 (0.73-1.00)	0.85 (0.74-0.99)	0.86 (0.77-0.95)
Lamotrigine	0.75 (0.66-0.86)	0.97 (0.86-1.10)	0.86 (0.79-0.94)
Valproic acid	0.89 (0.79-1.00)	0.99 (0.79-1.24)	0.91 (0.82-1.01)
MS polytherapy	1.09 (0.84-1.42)	1.06 (0.83-1.35)	1.07 (0.90-1.28)

Supplementary Table 3. Risk of psychiatric hospitalization associated with specific antipsychotics (AP) and specific antidepressants (AD), in between-individual models of the Finnish and Swedish cohorts, and in meta-analysis (MA). Adjusted Hazard Ratios (aHRs) with 95% Confidence Intervals (CIs). LAI= long-acting injectable antipsychotic.

	Finnish cohort	Swedish cohort	Fixed effects MA
Antipsychotics	aHR (95%CI)	aHR (95%CI)	aHR (95%CI)
Any LAI	0.96 (0.70-1.32)	0.72 (0.52-1.00)	0.84 (0.67-1.05)
Perphenazine	1.08 (1.95-1.23)	1.13 (0.78-1.64)	1.08 (0.96-1.23)
Risperidone	1.18 (1.10-1.27)	1.02 (0.91-1.15)	1.13 (1.07-1.20)
Quetiapine	1.13 (1.08-1.19)	1.12 (1.04-1.20)	1.13 (1.08-1.18)
Haloperidol	1.48 (1.15-1.90)	1.01 (0.83-1.23)	1.17 (1.00-1.36)
Olanzapine	1.27 (1.18-1.36)	1.11 (1.03-1.19)	1.18 (1.12-1.24)
Aripiprazole	1.48 (1.31-1.67)	1.03 (0.93-1.15)	1.21 (1.12-1.31)
Clozapine	1.27 (1.00-1.60)	1.11 (0.75-1.63)	1.22 (1.00-1.49)
Flupentixol	1.74 (1.24-2.46)	1.14 (0.92-1.41)	1.28 (1.07-1.54)
Levomepromazine	1.33 (1.20-1.48)	1.23 (1.02-1.49)	1.31 (1.20-1.43)
AP Polytherapy	1.47 (1.38-1.56)	1.32 (1.22-1.42)	1.41 (1.34-1.47)
Antidepressants			
Bupropion	0.83 (0.69-1.01)	0.82 (0.71-0.96)	0.83 (0.74-0.93)
Sertraline	0.88 (0.81-0.96)	0.92 (0.84-1.00)	0.90 (0.85-0.95)
Vortioxetine	0.88 (0.73-1.08)	0.95 (0.79-1.14)	0.92 (0.80-1.05)
Citalopram	0.93 (0.86-1.01)	0.91 (0.81-1.03)	0.92 (0.87-0.99)
Escitalopram	0.98 (0.91-1.06)	0.96 (0.88-1.05)	0.97 (0.92-1.03)
Paroxetine	1.00 (1.89-1.12)	1.01 (0.82-1.25)	1.00 (0.90-1.11)
Fluoxetine	0.99 (1.90-1.10)	1.04 (0.92-1.17)	1.01 (0.94-1.09)
Duloxetine	1.08 (1.95-1.23)	1.00 (0.90-1.11)	1.03 (0.95-1.12)
Venlafaxine	1.05 (0.99-1.11)	0.99 (0.91-1.08)	1.03 (0.98-1.08)
AD polytherapy	1.18 (1.12-1.24)	1.09 (1.02-1.15)	1.14 (1.10-1.19)
Amitriptyline	1.18 (1.99-1.40)	1.07 (0.81-1.41)	1.15 (0.99-1.33)
Mirtazapine	1.17 (1.10-1.25)	1.14 (1.06-1.24)	1.16 (1.10-1.22)

Analyses adjusted for age, sex, duration of first inpatient stay with diagnosis of psychotic depression (0 days for outpatients), whether person had previous non-psychotic depression, anxiety disorders (ICD-10 F40-F43), personality disorders (F60-F69), ADHD (F90), substance use disorders (F10-F19 or use of ATC N07B), suicide attempt (X60-X84, Y10-Y34), diabetes (E10-E14 or use of ATC A10), asthma/COPD (J44-J46), cancer (C00-C99), cardiovascular disease (I00-I99), main occupational activity during previous year before baseline (work vs. disability pension vs. sickness absence vs. unemployment vs. other), and prior use of clozapine, LAI, lithium or other mood stabilizers.

Supplementary Table 4. Risk of psychiatric hospitalization associated with specific antidepressants compared with non-use of antidepressants and specific antipsychotics compared with non-use of antipsychotics in fixed effects versus random effects meta-analysis (MA) based on within-individual Cox models of the Finnish and Swedish cohorts. LAI: any long-acting injectable antipsychotic.

	Fixed Effects MA aHR (95%CI)	Random Effects MA aHR (95%CI)
<i>Antidepressants</i>		
Bupropion	0.73 (0.63-0.85)	0.73 (0.63-0.85)
Vortioxetine	0.78 (0.63-0.96)	0.78 (0.63-0.96)
Venlafaxine	0.92 (0.86-0.98)	0.92 (0.86-0.98)
Sertraline	0.94 (0.87-1.02)	0.94 (0.80-1.10)
Amitriptyline	1.00 (0.85-1.17)	1.00 (0.85-1.18)
AD polytherapy	1.01 (0.96-1.06)	1.01 (0.96-1.06)
Duloxetine	1.02 (0.93-1.12)	1.02 (0.93-1.12)
Fluoxetine	1.02 (0.93-1.13)	1.02 (0.93-1.13)
Escitalopram	1.02 (0.94-1.10)	1.02 (0.94-1.10)
Paroxetine	1.03 (0.89-1.18)	1.03 (0.89-1.18)
Citalopram	1.04 (0.95-1.14)	1.05 (0.92-1.20)
Mirtazapine	1.13 (1.06-1.21)	1.13 (1.06-1.21)
<i>Antipsychotics</i>		
LAI	0.60 (0.45-0.80)	0.58 (0.33-1.02)
Clozapine	0.72 (0.57-0.91)	0.72 (0.57-0.91)
Haloperidol	0.84 (0.69-1.04)	0.88 (0.56-1.40)
Quetiapine	0.96 (0.91-1.01)	0.97 (0.89-1.05)
Levomepromazine	0.98 (0.88-1.09)	0.98 (0.87-1.12)
Olanzapine	0.99 (0.93-1.05)	0.99 (0.93-1.05)
Perphenazine	1.03 (0.88-1.20)	1.02 (0.87-1.20)
Rare AP	1.04 (0.92-1.17)	1.01 (0.81-1.25)
Aripiprazole	1.04 (0.94-1.14)	1.04 (0.94-1.14)
Risperidone	1.05 (0.97-1.13)	1.05 (0.97-1.13)
AP polytherapy	1.07 (1.01-1.13)	1.07 (1.01-1.14)
Flupentixol	1.27 (1.00-1.61)	1.30 (0.86-1.96)

Supplementary Table 5. Risk of psychiatric hospitalization associated with specific antidepressants compared with non-use of antidepressants and specific antipsychotics compared with non-use of antipsychotics among those who do not experience diagnostic conversion to bipolar disorder or schizophrenia during the follow-up, in fixed effects meta-analysis (MA) based on within-individual Cox models of the Finnish and Swedish cohorts. LAI: any long-acting injectable antipsychotic.

Exposure	Fixed Effects MA aHR (95%CI)
<i>Antidepressants</i>	
Vortioxetine	0.77 (0.62-0.96)
Bupropion	0.77 (0.66-0.90)
Sertraline	0.92 (0.84-1.01)
Venlafaxine	0.92 (0.86-0.99)
Amitriptyline	0.98 (0.81-1.17)
Paroxetine	0.98 (0.82-1.16)
AD polytherapy	1.01 (0.95-1.07)
Fluoxetine	1.05 (0.94-1.17)
Citalopram	1.06 (0.95-1.18)
Escitalopram	1.06 (0.97-1.16)
Duloxetine	1.09 (0.97-1.21)
Mirtazapine	1.16 (1.08-1.25)
<i>Antipsychotics</i>	
LAI	0.66 (0.47-0.92)
Clozapine	0.66 (0.49-0.87)
Haloperidol	0.79 (0.61-1.01)
Perphenazine	0.92 (0.77-1.11)
Quetiapine	0.98 (0.92-1.05)
Levomepromazine	0.99 (0.87-1.12)
Rare AP	1.00 (0.87-1.16)
Olanzapine	1.02 (0.95-1.09)
Risperidone	1.08 (0.99-1.18)
Aripiprazole	1.09 (0.98-1.22)
AP polytherapy	1.10 (1.03-1.17)
Flupentixol	1.17 (0.90-1.53)

Supplementary Table 6. Risk of psychiatric hospitalization associated with two-drug combinations of most common antipsychotics and antidepressants and use of antidepressant only or antipsychotic only, with reference to non-use of both antipsychotics and antidepressants in within-individual design, in the Finnish and Swedish cohorts. Adjusted Hazard Ratios (aHRs) with 95% Confidence Intervals (CIs). LAI= long-acting injectable antipsychotic. PY: person-years.

	Finnish cohort				Swedish cohort			
	Events	Users	PYs	aHR (95%CI)	Events	Users	PYs	aHR (95%CI)
Non-use of both	5045	14272	53351	reference	4811	10765	38121	reference
<i>Antipsychotic-antidepressant combinations</i>								
Amitriptyline-Olanzapine	7	45	59	0.28 (0.11-0.70)	27	76	41	0.53 (0.31-0.90)
Amitriptyline-Quetiapine	21	133	82	1.06 (0.58-1.93)	24	71	47	0.97 (0.53-1.79)
Amitriptyline-Risperidone	12	50	48	1.73 (0.71-4.21)	24	33	32	1.43 (0.75-2.71)
Fluoxetine-Levomepromazine	10	39	18	0.82 (0.36-1.87)	14	40	16	0.73 (0.37-1.43)
Fluoxetine-Olanzapine	50	204	130	1.10 (0.72-1.67)	54	257	206	1.23 (0.81-1.87)
Fluoxetine-Quetiapine	185	513	434	0.98 (0.78-1.23)	41	203	126	0.70 (0.46-1.06)
Fluoxetine-Risperidone	51	198	127	1.39 (0.89-2.18)	18	102	57	0.96 (0.49-1.88)
Fluoxetine-Aripiprazole	12	47	22	0.99 (0.44-2.23)	55	125	69	1.22 (0.84-1.79)
Citalopram-Levomepromazine	37	88	109	0.80 (0.53-1.21)	9	27	6	2.10 (0.70-6.35)
Citalopram-Perphenazine	40	176	140	1.05 (0.64-1.71)	5	12	15	1.39 (0.29-6.72)
Citalopram-Olanzapine	99	385	414	0.86 (0.62-1.19)	55	271	214	0.83 (0.53-1.31)
Citalopram-Quetiapine	248	947	1379	0.80 (0.65-0.97)	31	155	84	1.49 (0.85-2.63)
Citalopram-Risperidone	111	491	480	1.05 (0.78-1.43)	23	144	84	0.86 (0.46-1.63)
Paroxetine-Levomepromazine	15	39	20	0.57 (0.24-1.34)	10	19	5	1.44 (0.63-3.29)
Paroxetine-Olanzapine	47	114	79	0.96 (0.64-1.42)	19	79	75	1.23 (0.57-2.66)
Paroxetine-Quetiapine	77	242	319	0.85 (0.59-1.23)	16	65	79	0.83 (0.39-1.79)
Paroxetine-Risperidone	40	150	121	1.41 (0.85-2.33)	14	29	28	0.78 (0.35-1.75)
Sertraline-Levomepromazine	18	58	45	1.22 (0.65-2.27)	38	72	35	1.30 (0.75-2.27)
Sertraline-Perphenazine	18	111	154	0.85 (0.44-1.64)	5	21	11	0.69 (0.21-2.31)
Sertraline-Flupentixol	4	10	4	1.11 (0.31-4.00)	21	48	40	1.16 (0.54-2.49)
Sertraline-Olanzapine	83	362	372	0.84 (0.60-1.18)	188	834	623	1.14 (0.91-1.44)
Sertraline-Quetiapine	217	829	944	0.74 (0.60-0.91)	117	426	313	0.89 (0.68-1.18)

Sertraline- Risperidone	68	387	388	0.93 (0.63-1.37)	66	309	276	1.12 (0.77-1.64)
Sertraline- Aripiprazole	25	110	78	1.28 (0.71-2.32)	67	277	228	0.93 (0.67-1.29)
Escitalopram- Levomepromazine	17	58	28	0.96 (0.46-2.01)	4	38	27	0.40 (0.11-1.40)
Escitalopram- Perphenazine	27	118	102	1.17 (0.68-1.99)	3	12	6	0.98 (0.24-4.10)
Escitalopram- Olanzapine	141	595	456	0.94 (0.71-1.24)	123	558	375	0.82 (0.62-1.09)
Escitalopram- Quetiapine	454	1502	1399	1.03 (0.88-1.20)	104	377	322	1.16 (0.87-1.53)
Escitalopram- Risperidone	80	411	321	0.93 (0.66-1.32)	37	196	125	0.92 (0.57-1.46)
Escitalopram- Aripiprazole	28	140	97	1.03 (0.63-1.70)	36	189	131	0.88 (0.57-1.36)
Mirtazapine- Levomepromazine	38	136	96	0.98 (0.64-1.50)	12	111	55	0.66 (0.31-1.43)
Mirtazapine- Perphenazine	45	186	145	1.03 (0.63-1.68)	5	13	8	1.24 (0.33-4.67)
Mirtazapine- Olanzapine	168	704	595	0.88 (0.70-1.10)	241	898	557	1.20 (0.97-1.49)
Mirtazapine- Quetiapine	298	1241	1042	1.03 (0.86-1.23)	113	407	239	1.25 (0.96-1.63)
Mirtazapine- Risperidone	260	898	865	1.07 (0.88-1.30)	60	349	194	0.87 (0.59-1.27)
Mirtazapine- Aripiprazole	32	91	62	2.70 (1.52-4.80)	20	151	81	0.81 (0.45-1.48)
Bupropion- Olanzapine	11	108	81	0.42 (0.19-0.93)	24	116	68	0.83 (0.44-1.55)
Bupropion- Quetiapine	60	418	277	0.83 (0.56-1.22)	36	171	82	1.11 (0.66-1.85)
Venlafaxine- Levomepromazine	47	169	147	0.78 (0.53-1.16)	15	82	39	1.71 (0.83-3.52)
Venlafaxine- Perphenazine	38	191	206	0.98 (0.58-1.67)	5	18	10	0.72 (0.16-3.26)
Venlafaxine- Clozapine	19	28	35	0.59 (0.35-1.02)	2	6	8	0.60 (0.10-3.63)
Venlafaxine- Olanzapine	374	926	1136	0.78 (0.66-0.93)	200	694	529	1.05 (0.84-1.31)
Venlafaxine- Quetiapine	825	2010	2895	0.79 (0.70-0.90)	181	431	472	0.90 (0.73-1.12)
Venlafaxine- Risperidone	312	811	1021	1.12 (0.92-1.35)	97	270	223	1.14 (0.77-1.67)
Venlafaxine- Aripiprazole	82	252	243	0.97 (0.70-1.36)	39	217	167	0.76 (0.49-1.17)
Duloxetine- Levomepromazine	2	26	15	0.55 (0.12-2.58)	26	72	47	1.72 (0.95-3.09)
Duloxetine- Perphenazine	25	44	57	1.33 (0.73-2.43)	1	6	2	2.02 (0.13-32.59)
Duloxetine- Olanzapine	69	172	154	1.33 (0.93-1.92)	65	280	165	0.92 (0.65-1.29)
Duloxetine- Quetiapine	199	572	679	0.80 (0.64-0.99)	76	269	255	1.11 (0.80-1.53)
Duloxetine- Risperidone	15	95	103	1.17 (0.54-2.52)	28	120	64	1.79 (1.04-3.09)

Duloxetine-Aripiprazole	16	53	30	1.20 (0.61-2.37)	43	124	105	0.92 (0.61-1.39)
Vortioxetine-Olanzapine	11	65	24	0.82 (0.33-2.06)	11	50	27	0.95 (0.43-2.06)
Vortioxetine-Quetiapine	23	196	82	1.42 (0.73-2.77)	14	81	50	1.16 (0.56-2.42)
<i>Antidepressant only (without concomitant antipsychotic)</i>								
Vortioxetine	24	400	154	0.52 (0.28-1.00)	56	372	300	0.75 (0.49-1.14)
Bupropion	53	787	532	0.66 (0.43-1.02)	98	817	615	0.73 (0.56-0.95)
Duloxetine	123	1019	1008	0.89 (0.67-1.17)	278	1260	1546	0.90 (0.74-1.10)
Sertraline	255	1738	2088	0.81 (0.66-1.00)	646	3032	3796	0.95 (0.83-1.09)
Fluoxetine	170	1222	1310	0.86 (0.67-1.09)	384	1124	1389	0.98 (0.83-1.16)
Venlafaxine	644	3505	4981	0.99 (0.87-1.13)	566	2175	3389	0.90 (0.78-1.05)
Paroxetine	158	741	1016	0.96 (0.74-1.26)	94	320	437	1.10 (0.79-1.52)
Escitalopram	427	2871	2885	0.94 (0.80-1.10)	440	1980	2265	1.11 (0.95-1.30)
Amitriptyline	110	614	612	1.29 (0.94-1.76)	59	653	558	0.73 (0.49-1.07)
Citalopram	481	2459	3224	1.07 (0.91-1.25)	248	1325	1616	1.27 (1.01-1.59)
Mirtazapine	706	3873	3142	1.16 (1.02-1.32)	640	3086	2455	1.18 (1.04-1.35)
<i>Antipsychotic only (without concomitant antidepressant)</i>								
LAI	19	58	54	0.52 (0.27-1.00)	13	34	21	1.03 (0.51-2.07)
Clozapine	10	47	29	0.56 (0.27-1.14)	12	12	10	1.12 (0.50-2.51)
Haloperidol	15	82	25	1.41 (0.68-2.95)	12	129	35	0.52 (0.26-1.04)
Risperidone	165	1212	675	1.10 (0.87-1.40)	48	593	283	0.61 (0.40-0.91)
Quetiapine	774	3922	3555	0.89 (0.79-1.00)	269	1175	702	1.11 (0.93-1.32)
Levomepromazine	89	300	276	0.97 (0.72-1.30)	55	258	140	0.97 (0.68-1.38)
Perphenazine	48	405	189	1.10 (0.71-1.68)	4	36	15	0.90 (0.18-4.42)
Olanzapine	209	1306	857	1.28 (1.04-1.57)	171	1401	663	0.97 (0.78-1.21)
Aripiprazole	57	372	183	1.10 (0.77-1.58)	74	471	204	1.20 (0.86-1.68)
Flupentixol	10	51	24	3.38 (1.12-10.18)	15	121	75	0.88 (0.41-1.89)