**SUPPLEMENTARY MATERIAL**

**SUMMARY OF TABLES**

**Table 1s**. Association between covariates at the onset of the treatment episode and BAMM in the incident cohort

**Table 2s.** Medians and interquartile ranges for drug doses

**Table 3s.** Definition of covariates

**Table 4s**. Incidence of Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) and duration of treatment episode following a BAMM event in the prevalent cohort

**Figure 1s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous LAI treatment episode in individuals with a previous BAMM episode in the prevalent cohort

**Figure 2s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous OAP treatment episode in individuals with a previous BAMM episode in the prevalent cohort

**Figure 3s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous LAI treatment episode in the incident cohort

**Figure 4s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous OAP treatment episode in the incident cohort

**Table 5s.** Association between covariates occurring within the treatment episode and Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) in individuals with ≤ 2 different antipsychotic drugs tried for >6 weeks during their lifetime in the incident cohort (i.e., not meeting criteria for proxy of treatment resistant schizophrenia)

**Table 6s.** Sensitivity analyses comparing associations of covariates with Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) between events occurring in treatment episodes < median duration and events occurring ≥ median duration

**Table 7s.** Proportion of Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) and time to event by time since last hospitalization at treatment onset

**Table 8s.** Association between baseline characteristics in the prevalent cohort with a previous BAMM episode and a second BAMM event in the prevalent cohort

**Table 1s**. Association between covariates at the onset of the treatment episode and Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) in the incident cohort

|  |  |  |
| --- | --- | --- |
|  | LAI (N=1,748) | OAP (N=5,639) |
| Variable | BAMM (N,%)N=387 | NO BAMM (N,%) N=1,361 | Univariate HR (95% CI) | Multivariate HR (95% CI) | BAMM (N,%)N=1,445 | NO BAMM (N,%) N=4,194 | Univariate HR (95% CI) | Multivariate HR (95% CI) |
| **Sociodemographic variables** |
| Male Gender |

|  |
| --- |
| 240 |
| (62.3%) |

 |

|  |
| --- |
| 755 |
| (55.6%) |

 | 1.32(1.07-1.62) |  |

|  |
| --- |
| 2168 |
| (51.7%) |

 |

|  |
| --- |
| 857 |
| (59.5%) |

 | **1.30(1.17-1.44)** | 1.12(1.01-1.24) |
| Age |  |  |  |  |  |  |  |  |
| <=30 |

|  |
| --- |
| 140 |
| (36.3%) |

 |

|  |
| --- |
| 312 |
| (22.9%) |

 | 1.70(1.19-2.43) |  |

|  |
| --- |
| 713 |
| (49.5%) |

 |

|  |
| --- |
| 1303 |
| (31.1%) |

 | **2.32(1.90-2.83)** | **2.12(1.71-2.63)** |
| 31-40 |

|  |
| --- |
| 102 |
| (26.4%) |

 |

|  |
| --- |
| 347 |
| (25.5%) |

 | 1.09(0.75-1.58) |  |

|  |
| --- |
| 312 |
| (21.6%) |

 |

|  |
| --- |
| 905 |
| (21.6%) |

 | **1.49(1.20-1.86)** | 1.36(1.09-1.71) |
| 41-50 |

|  |
| --- |
| 68 |
| (17.6%) |

 |

|  |
| --- |
| 303 |
| (22.3%) |

 | 0.85(0.57-1.26) |  |

|  |
| --- |
| 180 |
| (12.5%) |

 |

|  |
| --- |
| 740 |
| (17.6%) |

 | 1.10(0.87-1.40) | 1.03(0.81-1.31) |
| 51-60 |

|  |
| --- |
| 36 |
| (9.3%) |

 |

|  |
| --- |
| 233 |
| (17.1%) |

 | 0.60(0.38-0.94) |  |

|  |
| --- |
| 122 |
| (8.4%) |

 |

|  |
| --- |
| 585 |
| (13.9%) |

 | 0.98(0.76-1.27) | 0.94(0.73-1.22) |
| >60\* |

|  |
| --- |
| 39 |
| (10.1%) |

 |

|  |
| --- |
| 163 |
| (12.0%) |

 | 1.0 | 1.0 |

|  |
| --- |
| 112 |
| (7.7%) |

 |

|  |
| --- |
| 655 |
| (15.6%) |

 | 1.0 | 1.0 |
| **Comorbidity**  |
| Substance use disorders |

|  |
| --- |
| 61 |
| (15.8%) |

 |

|  |
| --- |
| 239 |
| (17.6%) |

 | 1.06(0.81-1.40) |  |

|  |
| --- |
| 161 |
| (11.1%) |

 |

|  |
| --- |
| 569 |
| (13.5%) |

 | 1.09(0.92-1.28) |  |
| Suicidality |

|  |
| --- |
| 9 |
| (2.3%) |

 |

|  |
| --- |
| 8 |
| (0.5%) |

 | 2.5(1.30-4.88) |  |

|  |
| --- |
| 12 |
| (0.8%) |

 |

|  |
| --- |
| 31 |
| (0.7%) |

 | 1.29(0.73-2.28) |  |
| Cancer |

|  |
| --- |
| 4 |
| (1.0%) |

 |

|  |
| --- |
| 20 |
| (1.4%) |

 | 0.76(0.28-2.04) |  |

|  |
| --- |
| 16 |
| (1.1%) |

 |

|  |
| --- |
| 110 |
| (2.6%) |

 | 0.60(0.36-0.98) |  |
| Cardiovascular disease |

|  |
| --- |
| 31 |
| (8.0%) |

 |

|  |
| --- |
| 126 |
| (9.2%) |

 | 0.93(0.64-1.35) |  |

|  |
| --- |
| 94 |
| (6.5%) |

 |

|  |
| --- |
| 509 |
| (12.1%) |

 | **0.68(0.55-0.84)** | 0.91(0.73-1.14) |
| Intellectual disability |

|  |
| --- |
| 5 |
| (1.3%) |

 |

|  |
| --- |
| 29 |
| (2.1%) |

 | 0.53(0.22-1.29) |  |

|  |
| --- |
| 23 |
| (1.6%) |

 |

|  |
| --- |
| 79 |
| (1.8%) |

 | 0.75(0.49-1.13) |  |
| Cognitive disorders |

|  |
| --- |
| 0 |
| (0.0%) |

 |

|  |
| --- |
| 6 |
| (0.4%) |

 |  |  |

|  |
| --- |
| 4 |
| (0.2%) |

 |

|  |
| --- |
| 40 |
| (0.9%) |

 | 0.40(0.15-1.07) |  |
| Tardive dyskinesia |

|  |
| --- |
| 1 |
| (0.2%) |

 |

|  |
| --- |
| 1 |
| (0.1%) |

 | 4.00(0.56-28.55) |  |

|  |
| --- |
| 0 |
| (0.0%) |

 |

|  |
| --- |
| 2 |
| (0.0%) |

 |  |  |
| Diabetes |

|  |
| --- |
| 8 |
| (2.0%) |

 |

|  |
| --- |
| 38 |
| (2.8%) |

 | 0.75(0.37-1.51) |  |

|  |
| --- |
| 14 |
| (0.9%) |

 |

|  |
| --- |
| 88 |
| (2.1%) |

 | 0.52(0.31-0.89) |  |
| Asthma |

|  |
| --- |
| 13 |
| (3.3%) |

 |

|  |
| --- |
| 48 |
| (3.5%) |

 | 1.06(0.81-1.40) |  |

|  |
| --- |
| 41 |
| (2.8%) |

 |

|  |
| --- |
| 138 |
| (3.3%) |

 | 1.09(0.93-1.28) |  |
| **Illness characteristics** |
| Disease duration |
| <=5 years |

|  |
| --- |
| 276 |
| (71.6%) |

 |

|  |
| --- |
| 999 |
| (73.5%) |

 | 1.0 |  |

|  |
| --- |
| 1361 |
| (94.5%) |

 |

|  |
| --- |
| 3839 |
| (91.6%) |

 | 1.0 |  |
| 5-15 years |

|  |
| --- |
| 104 |
| (27.0%) |

 |

|  |
| --- |
| 332 |
| (24.4%) |

 | 0.92(0.38-2.25) |  |

|  |
| --- |
| 77 |
| (5.3%) |

 |

|  |
| --- |
| 325 |
| (7.7%) |

 | 3.70(0.53-26.10) |  |
| >15 years\* |

|  |
| --- |
| 5 |
| (1.3%) |

 |

|  |
| --- |
| 27 |
| (1.9%) |

 | 1.03(0.42-2.53) |  |

|  |
| --- |
| 1 |
| (0.1%) |

 |

|  |
| --- |
| 24 |
| (0.5%) |

 | 3.02(0.42-21.59) |  |
| Type of psychotic disorder in the latest hospitalization |
| Schizophrenia |

|  |
| --- |
| 313 |
| (81.3%) |

 |

|  |
| --- |
| 1104 |
| (81.3%) |

 | 0.80(0.50-1.27) |  |

|  |
| --- |
| 1058 |
| (73.5%) |

 |

|  |
| --- |
| 3364 |
| (80.3%) |

 | 1.06(0.82-1.38) |  |
| Schizoaffective disorder |

|  |
| --- |
| 53 |
| (13.7%) |

 |

|  |
| --- |
| 184 |
| (13.5%) |

 | 0.92(0.54-1.59) |  |

|  |
| --- |
| 246 |
| (17.1%) |

 |

|  |
| --- |
| 563 |
| (13.4%) |

 | 1.01(0.76-1.34) |  |
| Other psychoses\* |

|  |
| --- |
| 19 |
| (4.9%) |

 |

|  |
| --- |
| 70 |
| (5.1%) |

 | 1.0 |  |

|  |
| --- |
| 135 |
| (9.3%) |

 |

|  |
| --- |
| 261 |
| (6.2%) |

 | 1.0 |  |
| **Treatment history**  |
| Number of previous hospitalizations |
| 0-3 \*  |

|  |
| --- |
| 160 |
| (41.5%) |

 |

|  |
| --- |
| 735 |
| (54.1%) |

 | 1.0 | 1.0 |

|  |
| --- |
| 1058 |
| (73.5%) |

 |

|  |
| --- |
| 3364 |
| (80.3%) |

 | 1.0 | 1.0 |
| 4-6  |

|  |
| --- |
| 97 |
| (25.1%) |

 |

|  |
| --- |
| 354 |
| (26.0%) |

 | 1.23(0.95-1.58) | 1.21(0.94-1.56) |

|  |
| --- |
| 246 |
| (17.1%) |

 |

|  |
| --- |
| 563 |
| (13.4%) |

 | **1.41(1.23-1.62)** | **1.53(1.33-1.76)** |
| >6  |

|  |
| --- |
| 128 |
| (33.2%) |

 |

|  |
| --- |
| 269 |
| (19.8%) |

 | **2.12(1.68-2.67)** | **2.00(1.58-2.53)** |

|  |
| --- |
| 135 |
| (9.3%) |

 |

|  |
| --- |
| 261 |
| (6.2%) |

 | **1.85(1.55-2.22)** | **2.04(1.70-2.44)** |
| Time since hospital discharge |
| <2 months |

|  |
| --- |
| 338 |
| (87.7%) |

 |

|  |
| --- |
| 1122 |
| (82.6%) |

 | 1.61(1.01-2.55) |  |

|  |
| --- |
| 1202 |
| (83.5%) |

 |

|  |
| --- |
| 3060 |
| (73.0%) |

 | **2.18(1.72-2.77)** | **2.03(1.60-2.58)** |
| 2-12 months |

|  |
| --- |
| 28 |
| (7.2%) |

 |

|  |
| --- |
| 133 |
| (9.7%) |

 | 1.20(0.67-2.15) |  |

|  |
| --- |
| 165 |
| (11.4%) |

 |

|  |
| --- |
| 554 |
| (13.2%) |

 | **2.05(1.55-2.70)** | **1.96(1.49-2.59)** |
| >12 months\* |

|  |
| --- |
| 19 |
| (4.9%) |

 |

|  |
| --- |
| 103 |
| (7.5%) |

 | 1.0 |  |

|  |
| --- |
| 72 |
| (5.0%) |

 |

|  |
| --- |
| 574 |
| (13.7%) |

 | 1.0 |  |
| **Co-treatment**  |
| Antidepressants  |

|  |
| --- |
| 84 |
| (21.8%) |

 |

|  |
| --- |
| 184 |
| (13.5%) |

 | **1.69(1.33-2.15)** | **1.57(1.23-2.00)** |

|  |
| --- |
| 354 |
| (24.6%) |

 |

|  |
| --- |
| 1036 |
| (24.7%) |

 | 1.01(0.90-1.14) |  |
| Benzodiazepines  |

|  |
| --- |
| 82 |
| (21.3%) |

 |

|  |
| --- |
| 194 |
| (14.2%) |

 | **1.54(1.21-1.97)** | 1.31(1.02-1.69) |

|  |
| --- |
| 283 |
| (19.6%) |

 |

|  |
| --- |
| 768 |
| (18.3%) |

 | 1.16(1.02-1.33) |  |
| Z-drugs  |

|  |
| --- |
| 23 |
| (5.9%) |

 |

|  |
| --- |
| 79 |
| (5.8%) |

 | 1.06(0.69-1.61) |  |

|  |
| --- |
| 84 |
| (5.8%) |

 |

|  |
| --- |
| 299 |
| (7.1%) |

 | 0.91(0.73-1.13) |  |
| Antiparkinsonian drugs  |

|  |
| --- |
| 40 |
| (10.3%) |

 |

|  |
| --- |
| 120 |
| (8.8%) |

 | 1.15(0.83-1.60) |  |

|  |
| --- |
| 65 |
| (4.5%) |

 |

|  |
| --- |
| 149 |
| (3.5%) |

 | 1.21(0.94-1.55) |  |
| Lithium  |

|  |
| --- |
| 16 |
| (4.1%) |

 |

|  |
| --- |
| 43 |
| (3.1%) |

 | 1.49(0.90-2.46) |  |

|  |
| --- |
| 50 |
| (3.4%) |

 |

|  |
| --- |
| 126 |
| (3.0%) |

 | 1.11(0.84-1.47) |  |
| Mood stabilizers |

|  |
| --- |
| 35 |
| (9.0%) |

 |

|  |
| --- |
| 118 |
| (8.6%) |

 | 1.18(0.83-1.67) |  |

|  |
| --- |
| 137 |
| (9.5%) |

 |

|  |
| --- |
| 430 |
| (10.2%) |

 | 0.94(0.79-1.12) |  |
| Addiction pharmacotherapy  |

|  |
| --- |
| 9 |
| (2.3%) |

 |

|  |
| --- |
| 18 |
| (1.3%) |

 | 1.55(0.80-3.00) |  |

|  |
| --- |
| 16 |
| (1.1%) |

 |

|  |
| --- |
| 52 |
| (1.2%) |

 | 1.22(0.75-2.00) |  |

\*Reference. Significant results after Bonferroni correction (p<0.00217) are bolded

**Table 2s.** Medians and interquartile ranges in DDD of cumulative drug doses per patient/day among individuals who received at least a prescription in the incident cohort

|  |  |  |
| --- | --- | --- |
|  | **LAI** | **OAP** |
| **Drug** | **Median** | **1st Quartile** | **4th quartile** | **Median** | **1st Quartile** | **4th quartile** |
| Antipsychotics | 1.22 | 0.88 | 1.95 | 0.97 | 0.52 | 1.61 |
| Antidepressants | 0.92 | 0.38 | 1.04 | 0.91 | 0.45 | 1.44 |
| Benzodiazepines | 0.61 | 0.21 | 1.17 | 0.51 | 0.18 | 1.08 |
| Z-Drugs | 0.46 | 0.10 | 0.97 | 0.48 | 0.15 | 0.98 |
| Antiparkinsonian | 0.19 | 0.07 | 0.34 | 0.12 | 0.5 | 0.23 |
| Lithium | 0.91 | 0.45 | 1.26 | 0.86 | 0.61 | 1.15 |
| Mood stabilizers | 0.49 | 0.26 | 0.74 | 0.54 | 0.33 | 0.75 |
| Addiction pharmacotherapy | 0.64 | 0.26 | 0.91 | 0.36 | 0.12 | 0.80 |

**Table 3s.** Definition of covariates

|  |  |  |  |
| --- | --- | --- | --- |
| **Definition** | **ICD-code/ATC-code/ categorization** | **Measurement period** | **Data source** |
| **COHORT MODEL** |
| Age, years | Categorized as: <=30, 31-40, 41-50, 51-60, >60 (the reference category) | At the start of treatment episode | FCR |
| Gender | MaleFemale (the reference category) |  | FCR |
| **Comorbidities** |  |  |  |
| Substance abuse disorder | Hospitalization (ICD-10: F10-F19, K86.0, K70; ICD-9: 291, 292, 2940A, 303, 304, 305, 5770D-F, 5771C, 5771D, 5710A, 5711A, 5712A, 5713X; ICD-8: 291, 303, 304, 57700-57708); ***or*** medication use (ATC-codes N07BB, N07BC01, N07BC02, N07BC5) | Diagnosed since 1972 until the start of treatment episode, or drugs used since 1995 until the start of treatment episode | FCR, PR |
| Suicidality | ICD-10: X60–X84, Y10–Y34, Z72.8, Z91.5; ICD-9: E950A, E954A, E955A, E956A, E957A, E959A, E959X, E970A, E972A, E973A, E974A, E979A; ICD-8: E950-E959 | Diagnosed since 1972 until the start of treatment episode | FCR |
| Post-traumatic stress disorder, PTSD | ICD-10: F43.1; ICD-9: 309.8X | Diagnosed since 1972 until the start of treatment episode | FCR |
| Cancer | ICD-10: C00–C99; ICD-9: 140-208; ICD-8: 140-208 | Diagnosed since 1972 until the start of treatment episode | FCR |
| Cardiovascular disease | ICD-10: I00–I99; ICD-9: 40-45; ICD-8: 40-45 | Diagnosed since 1972 until the start of treatment episode | FCR |
| Intellectual disability | ICD-10: F70-F79; ICD-9: 317-319; ICD-8:310-315  | Diagnosed since 1972 until the start of treatment episode | FCR |
| Cognitive disorders | ICD-10: F00-F03, G30-G31;ICD-9: 290, 3310, 3311, 3312, 3318, 3334, 4378; ICD-8: 290, 437, 33100 | Diagnosed since 1972 until the start of treatment episode | FCR |
| Tardive dyskinesia | ICD-10: G24.0; ICD-9: 333.85  | Diagnosed since 1972 until the start of treatment episode | FCR |
| Diabetes | ICD-10: E10-E14;ICD-9: 250;ICD-8: 250 | Diagnosed since 1972 until the start of treatment episode | FCR |
| Asthma/ COPD | ICD-10: J44-J46;ICD-9: 493, 496;ICD-8: 493 | Diagnosed since 1972 until the start of treatment episode | FCR |
| **Treatment history upon onset of treatment episode** |
| Duration of illness, years | ≤5, 5-15, >15 (the reference category)  | At the start of treatment episode | FCR |
| Type of psychotic disorder | Categorized as schizophrenia (ICD-10: F20; ICD-9: 295.0-6; ICD-8: 295.0-6),schizoaffective disorder (ICD-10: F25; ICD-9: 295.7; ICD-8: 295.7), other primary psychoses (ICD-10: the rest of F20-29; ICD-9: 295.8-9; ICD-8: 295.8-9) | Diagnoses recorded in the last psychiatric hospitalization before the start of treatment episode | FCR |
| Number of previous hospitalizations for psychosis | Categorized as: 0-3 (the reference category), 4-6, >6.ICD-10: F20-F29  | At the start of treatment episode | FCR |
| Time since last hospital discharge | Categorized as: ≤2, 2-12, >12 months | At the start of treatment episode | FCR |
| **Baseline pharmacological treatment** |
| Antidepressant | N06A | Within 14 days before the start of treatment episode | PR |
| Antiparkinsonian | N04AA | Within 14 days before the start of treatment episode | PR |
| Benzodiazepine | N05BA, N05CD | Within 14 days before the start of treatment episode | PR |
| Z-drugs | N05CF | Within 14 days before the start of treatment episode | PR |
| Lithium | N05AN01 | Within 14 days before the start of treatment episode | PR |
| Mood stabilizer | Carbamazepine N03AF01, Valproic acid N03AG01, Lamotrigine N03AX09 | Within 14 days before the start of treatment episode | PR |
| Pharmacotherapy for substance dependence | Drugs for alcohol dependence N07BB, buprenorphine N07BC01, methadone N07BC02, buprenorphine with naloxone N07BC51 | Within 14 days before the start of treatment episode | PR |
| **Cumulative DDD at baseline** |
| Absolute sum of DDDs | For each drug class as described in “baseline pharmacological treatment” section; categorized as quartiles; calculated only for incident cases | Between the date of first prescription and the start of treatment episode | PR |
| Relative dose  | Absolute sum of DDDs divided by the time between date of first prescription and start of treatment episode.For each drug class as described in “baseline pharmacological treatment” section; categorized as quartiles; calculated only for incident cases | Between the date of first prescription and the start of treatment episode | PR |
| **CASE-CONTROL MODEL** |
| Age, years | Categorized as: <=30, 31-40, 41-50, 51-60, >60 (the reference category) | At the end of treatment episode (BAMM or matching date) | FCR |
| Gender |  |  | FCR |
| **Treatment history upon onset of treatment episode** |
| Number of previous hospitalizations for psychosis | Categorized as: 0-3 (the reference category), 4-6, >6.ICD-10: F20-F29  | At the start of treatment episode | FCR |
| Time since last hospital discharge | Categorized as: ≤2, 2-12, >12 months | At the start of treatment episode | FCR |
| Comorbid conditions | Defines as described in “comorbidities” section above | At the end of treatment episode (BAMM or matching date) |  |
| **Treatment episode characteristics** |
| Antipsychotic type being prescribed at the end of treatment episode | Categorized as FGA, SGA, combination of these | At the end of treatment episode (BAMM or matching date) | PR |
| Duration of treatment episode | Categorized as 2-6, 6-12, >12 months | At the end of treatment episode (BAMM or matching date) | PR |
| **Dose during the treatment episode** |
| Cumulative sum of DDDs divided by duration of treatment episode; Antipsychotic Antidepressant Antiparkinsonian Benzodiazepine Z-drugs Lithium Mood stabilizer Pharmacotherapy for substance dependence | Categorized into quartiles among those who used the particular drug;drugs defined as in the section “baseline pharmacological treatment” above | During the treatment episode | PR |
| Antidepressants  | ATC=N06A | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Benzodiazepines  | ATC=N05BA, N05CD | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Antiparkinsonian medications  | ATC=N04AA | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Z-drugs  | (ATC= N05CF, i.e., zaleplon, zolpidem,, zopiclone, etc), | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| lithium  | ATC= N05AN01 | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Mood stabilizers  | Carbamazepine: ATC=N03AF01, Valproic acid: ATC=N03AG01, and lamotrigine: ATC=N03AX09 | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Pharmacotherapy for substance dependence  | medications for alcohol dependence: ATC=N07BB, buprenorphine: ATC=N07BC01, methadone: ATC=N07BC02, buprenorphine with naloxone: ATC=N07BC51 | At baseline in cohort models and during the treatment episode in case-control models  | PR |
| Abbreviations: ATC, Anatomical Therapeutic Chemical; COPD, chronic obstructive pulmonary disease; FCR, Finnish Care Register; ICD, International Classification of Diseases; PR, Prescription Register; BAMM: Breakthrough on Antipsychotic Maintenance Medication; FGA: first-generation antipsychotic, SGA: second-generation antipsychotic. |

**Table 4s**. Incidence of Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) and duration of treatment episode following a BAMM event in the prevalent cohort

|  |  |  |
| --- | --- | --- |
|  | LAI (N=4,230) | OAP (N=9,953) |
| Incidence rate per 10 person-years (95%CI) | 3.32 (3.31-3.34) | 2.22 (2.22-2.23) |
| Cumulative probability of BAMM | 49.7% | 53.5% |
| Treatment duration in days, (median, IQR) | 226.5, (110-640)\* | 352, (142-1093)\* |
|  BAMM (median, IQR) | 172, (96-394) | 238, (116-623) |
|  No BAMM (median, IQR) | 338.5, (139-982) | 599, (202-1867) |

\* p Value between BAMM and no BAMM < 0.001

**Figure 1s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous LAI treatment episode in individuals with a previous BAMM episode in the prevalent cohort



**Figure 2s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous OAP treatment episode in individuals with a previous BAMM episode in the prevalent cohort



**Figure 3s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous LAI treatment episode in the incident cohort



**Figure 4s.** Kaplan-Meier survival curves for time to Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) during continuous OAP treatment episode in the incident cohort



**Table 5s.** Association between covariates occurring within the treatment episode and Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) in individuals with ≤ 2 different antipsychotic drugs tried for >6 weeks during their lifetime in the incident cohort (i.e., not meeting criteria for proxy of treatment resistant schizophrenia)

|  |  |  |
| --- | --- | --- |
|  | LAI (N=1,236) | OAP (N=5,195) |
|  | BAMM N (%) (N=256)  | No BAMM N (%) (N=980)  | Univariate HR (95% CI) | Multivariate HR (95% CI) | BAMM N (%) (N=1,312)  | No BAMM N (%) (N=3,883)  | Univariate HR (95% CI) | Multivariate HR (95% CI) |
| **Sociodemographic and baseline variables** |
| Male gender |

|  |
| --- |
| 159 |
| (62.1%) |

 |

|  |
| --- |
| 538 |
| (54.9%) |

 | **1.33(1.03-1.71)** | 1.14(0.87-1.50) |

|  |
| --- |
| 780 |
| (59.4%) |

 |

|  |
| --- |
| 2001 |
| (51.5%) |

 | **1.29(1.16-1.44)** | **1.14(1.02-1.27)** |
| Age <=30 |

|  |
| --- |
| 106 |
|  (41.4%) |

 |

|  |
| --- |
| 234 |
| (23.9%) |

 | **2.01(1.31-3.08)** | **1.62(1.01-2.60)** |

|  |
| --- |
| 672 |
| (51.2%) |

 |

|  |
| --- |
| 1249 |
| (32.2%) |

 | **2.35(1.91-2.90)** | **2.03(1.62-2.54)** |
| Age 31-40 |

|  |
| --- |
| 57 |
|  (22.3%) |

 |

|  |
| --- |
| 230 |
| (23.5%) |

 | 1.05(0.66-1.67) | 0.86(0.52-1.42) |

|  |
| --- |
| 276 |
| (21.0%) |

 |

|  |
| --- |
| 825 |
| (21.2%) |

 | **1.49(1.19-1.88)** | **1.33(1.04-1.69)** |
| Age 41-50 |

|  |
| --- |
| 44 |
|  (17.2%) |

 |

|  |
| --- |
| 207 |
| (21.1%) |

 | 0.94(0.58-1.52) | 0.77(0.46-1.29) |

|  |
| --- |
| 158 |
| (12.0%) |

 |

|  |
| --- |
| 672 |
| (17.3%) |

 | 1.10(0.86-1.42) | 0.99(0.77-1.29) |
| Age 51-60 |

|  |
| --- |
| 23 |
|  (9.0%) |

 |

|  |
| --- |
| 177 |
| (18.1%) |

 | 0.61(0.35-1.07) | **0.50(0.28-0.90)** |

|  |
| --- |
| 106 |
| (8.1%) |

 |

|  |
| --- |
| 532 |
| (13.7%) |

 | 0.98(0.75-1.29) | 0.92(0.70-1.21) |
| Age >60\* |

|  |
| --- |
| 26 |
|  (10.1%) |

 |

|  |
| --- |
| 132 |
| (13.5%) |

 |  |  |

|  |
| --- |
| 100 |
| (7.6%) |

 |

|  |
| --- |
| 605 |
| (15.6%) |

 |  |  |
| 0-3 previous hospitalizations\*  |

|  |
| --- |
| 141 |
|  (55.1%) |

 |

|  |
| --- |
| 630 |
| (64.3%) |

 |  |  |

|  |
| --- |
| 1025 |
| (78.1%) |

 |

|  |
| --- |
| 3214 |
| (82.8%) |

 |  |  |
| 4-6 previous hospitalizations  |

|  |
| --- |
| 62 |
|  (24.2%) |

 |

|  |
| --- |
| 222 |
| (22.6%) |

 | 1.21(0.90-1.63) | 1.15(0.84-1.58) |

|  |
| --- |
| 200 |
| (15.2%) |

 |

|  |
| --- |
| 486 |
| (12.5%) |

 | **1.32(1.13-1.54)** | **1.29(1.10-1.52)** |
| >6 previous hospitalizations |

|  |
| --- |
| 53 |
|  (20.7%) |

 |

|  |
| --- |
| 128 |
| (13.1%) |

 | **1.84(1.34-2.53)** | **2.03(1.43-2.90)** |

|  |
| --- |
| 87 |
| (6.6%) |

 |

|  |
| --- |
| 183 |
| (4.7%) |

 | **1.64(1.32-2.04)** | **1.60(1.28-2.01)** |
| Last hospital discharge <2 months |

|  |
| --- |
| 227 |
|  (88.7%) |

 |

|  |
| --- |
| 830 |
| (84.7%) |

 | 1.39(0.76-2.55) | 1.347(0.71-2.3) |

|  |
| --- |
| 1114 |
| (84.9%) |

 |

|  |
| --- |
| 2898 |
| (74.6%) |

 | **2.26(1.73-2.95)** | **2.33(1.78-3.05)** |
| Last hospital discharge 2-12 months |

|  |
| --- |
| 18 |
|  (7.0%) |

 |

|  |
| --- |
| 96 |
| (9.8%) |

 | 0.99(0.47-2.10) | 0.81(0.37-1.76) |

|  |
| --- |
| 141 |
| (10.7%) |

 |

|  |
| --- |
| 497 |
| (12.8%) |

 | **2.07(1.52-2.82)** | **2.07(1.52-2.82)** |
| Last hospital discharge <12 months\* |

|  |
| --- |
| 11 |
|  (4.3%) |

 |

|  |
| --- |
| 54 |
| (5.5%) |

 |  |  |

|  |
| --- |
| 57 |
| (4.3%) |

 |

|  |
| --- |
| 488 |
| (12.6%) |

 |  |  |
| **Comorbidities diagnosed before treatment episode** |
| Substance use disorders |

|  |
| --- |
| 30 |
|  (11.7%) |

 |

|  |
| --- |
| 143 |
| (14.5%) |

 | 0.97(0.66-1.42) |  |

|  |
| --- |
| 132 |
| (10.1%) |

 |

|  |
| --- |
| 485 |
| (12.4%) |

 | 1.08(0.90-1.29) |  |
| Suicidality |

|  |
| --- |
| 6 |
|  (2.3%) |

 |

|  |
| --- |
| 5 |
| (0.5%) |

 | **2.73(1.21-6.15)** | **3.039(1.3-7.106)** |

|  |
| --- |
| 12 |
| (0.9%) |

 |

|  |
| --- |
| 28 |
| (0.7%) |

 | 1.48(0.84-2.62) | 1.79(0.10-3.18) |
| Cancer |

|  |
| --- |
| 2 |
|  (0.7%) |

 |

|  |
| --- |
| 15 |
| (1.5%) |

 | 0.64(0.16-2.58) |  |

|  |
| --- |
| 11 |
| (0.8%) |

 |

|  |
| --- |
| 99 |
| (2.5%) |

 | **0.48(0.26-0.87)** | 0.72(0.39-1.31) |
| Cardiovascular disease |

|  |
| --- |
| 16 |
|  (6.2%) |

 |

|  |
| --- |
| 91 |
| (9.2%) |

 | 0.77(0.46-1.27) |  |

|  |
| --- |
| 78 |
| (5.9%) |

 |

|  |
| --- |
| 470 |
| (12.1%) |

 | **0.64(0.51-0.80)** | 0.89(0.69-1.13) |
| Intellectual disability |

|  |
| --- |
| 4 |
|  (1.5%) |

 |

|  |
| --- |
| 21 |
| (2.1%) |

 | 0.60(0.22-1.61) |  |

|  |
| --- |
| 23 |
| (1.7%) |

 |

|  |
| --- |
| 71 |
| (1.8%) |

 | 0.82(0.54-1.24) |  |
| Cognitive disorders |

|  |
| --- |
| 0 |
|  (0.0%) |

 |

|  |
| --- |
| 3 |
| (0.3%) |

 | 1.0 |  |

|  |
| --- |
| 3 |
| (0.2%) |

 |

|  |
| --- |
| 39 |
| (1.0%) |

 | **0.32(0.10-0.99)** |  |
| Tardive dyskinesia |

|  |
| --- |
| 1 |
|  (0.3%) |

 |

|  |
| --- |
| 0 |
| (0.0%) |

 | 1.0 |  |

|  |
| --- |
| 0 |
| (0.0%) |

 |

|  |
| --- |
| 2 |
| (0.1%) |

 | 1.0 |  |
| Diabetes |

|  |
| --- |
| 2 |
|  (0.7%) |

 |

|  |
| --- |
| 25 |
| (2.5%) |

 | 0.29(0.07-1.18) |  |

|  |
| --- |
| 11 |
| (0.8%) |

 |

|  |
| --- |
| 79 |
| (2.0%) |

 | **0.48(0.26-0.87)** |  |
| Asthma |

|  |
| --- |
| 6 |
|  (2.3%) |

 |

|  |
| --- |
| 34 |
| (3.4%) |

 | 0.69(0.31-1.56) |  |

|  |
| --- |
| 36 |
| (2.7%) |

 |

|  |
| --- |
| 124 |
| (3.1%) |

 | 1.01(0.72-1.41) |  |
| **Co-treatment at baseline** |
| Antidepressants  |

|  |
| --- |
| 56 |
|  (21.9%) |

 |

|  |
| --- |
| 109 |
| (11.1%) |

 | **1.94(1.44-2.61)** | **1.63(1.20-2.22)** |

|  |
| --- |
| 323 |
| (24.6%) |

 |

|  |
| --- |
| 953 |
| (24.5%) |

 | 1.04(0.92-1.17) | 1.02(0.90-1.16) |
| Benzodiazepines  |

|  |
| --- |
| 35 |
|  (13.7%) |

 |

|  |
| --- |
| 109 |
| (11.1%) |

 | 1.22(0.85-1.74) |  |

|  |
| --- |
| 239 |
| (18.2%) |

 |

|  |
| --- |
| 677 |
| (17.4%) |

 | 1.14(0.99-1.32) |  |
| z-drugs  |

|  |
| --- |
| 15 |
|  (5.8%) |

 |

|  |
| --- |
| 49 |
| (5.0%) |

 | 1.32(0.78-2.23) |  |

|  |
| --- |
| 69 |
| (5.3%) |

 |

|  |
| --- |
| 261 |
| (6.7%) |

 | 0.89(0.70-1.14) |  |
| Antiparkinsonian drugs  |

|  |
| --- |
| 28 |
|  (10.9%) |

 |

|  |
| --- |
| 94 |
| (9.6%) |

 | 1.14(0.77-1.68) |  |

|  |
| --- |
| 53 |
| (4.0%) |

 |

|  |
| --- |
| 131 |
| (3.3%) |

 | 1.16(0.88-1.53) |  |
| Lithium  |

|  |
| --- |
| 8 |
|  (3.1%) |

 |

|  |
| --- |
| 27 |
| (2.7%) |

 | 1.44(0.71-2.93) |  |

|  |
| --- |
| 43 |
| (3.3%) |

 |

|  |
| --- |
| 109 |
| (2.8%) |

 | 1.12(0.82-1.52) |  |
| Mood stabilizers |

|  |
| --- |
| 16 |
|  (6.2%) |

 |

|  |
| --- |
| 72 |
| (7.3%) |

 | 0.97(0.58-1.61) |  |

|  |
| --- |
| 123 |
| (9.4%) |

 |

|  |
| --- |
| 382 |
| (9.8%) |

 | 0.98(0.81-1.18) |  |
| Addiction pharmacotherapy |

|  |
| --- |
| 4 |
|  (1.5%) |

 |

|  |
| --- |
| 9 |
| (0.9%) |

 | 1.77(0.65-4.75) |  |

|  |
| --- |
| 14 |
| (1.1%) |

 |

|  |
| --- |
| 45 |
| (1.1%) |

 | 1.30(0.76-2.20) |  |
| **Cumulative drug dose at baseline** |
| Antipsychotics (No use)\* |

|  |
| --- |
| 91 |
|  (35.5%) |

 |

|  |
| --- |
| 348 |
| (35.5%) |

 | 1.0 |  |

|  |
| --- |
| 707 |
| (53.8%) |

 |

|  |
| --- |
| 2119 |
| (54.5%) |

 | 1.0 |  |
| Antipsychotics (1st Quartile) |

|  |
| --- |
| 35 |
|  (13.6%) |

 |

|  |
| --- |
| 200 |
| (20.4%) |

 | 0.72(0.49-1.07) | 0.67(0.44-1.01) |

|  |
| --- |
| 122 |
| (9.3%) |

 |

|  |
| --- |
| 516 |
| (13.2%) |

 | 0.83(0.68-1.00) | 0.94(0.78-1.15) |
| Antipsychotics (2nd Quartile) |

|  |
| --- |
| 34 |
|  (13.2%) |

 |

|  |
| --- |
| 187 |
| (19.0%) |

 | 0.78(0.53-1.16) | 0.68(0.45-1.04) |

|  |
| --- |
| 143 |
| (10.9%) |

 |

|  |
| --- |
| 445 |
| (11.4%) |

 | 1.04(0.87-1.25) | 1.12(0.93-1.3) |
| Antipsychotics (3rd Quartile) |

|  |
| --- |
| 46 |
|  (17.9%) |

 |

|  |
| --- |
| 126 |
| (12.8%) |

 | 1.32(0.92-1.88) | 1.01(0.69-1.49) |

|  |
| --- |
| 137 |
| (10.4%) |

 |

|  |
| --- |
| 405 |
| (10.4%) |

 | 1.06(0.88-1.27) | 1.17(0.96-1.42) |
| Antipsychotics (4th Quartile) |

|  |
| --- |
| 50 |
|  (19.5%) |

 |

|  |
| --- |
| 119 |
| (12.1%) |

 | **1.52(1.07-2.14)** | 1.29(0.90-1.86) |

|  |
| --- |
| 203 |
| (15.4%) |

 |

|  |
| --- |
| 398 |
| (10.2%) |

 | **1.50(1.29-1.76)** | **1.55(1.32-1.82)** |
| Antidepressants (No use)\* |

|  |
| --- |
| 152 |
|  (59.3%) |

 |

|  |
| --- |
| 663 |
| (67.6%) |

 | 1.0 |  |

|  |
| --- |
| 855 |
| (65.1%) |

 |

|  |
| --- |
| 2432 |
| (62.6%) |

 | 1.0 |  |
| Antidepressants (1st Quartile) |

|  |
| --- |
| 17 |
|  (6.6%) |

 |

|  |
| --- |
| 95 |
| (9.6%) |

 | 0.89(0.53-1.47) |  |

|  |
| --- |
| 107 |
| (8.1%) |

 |

|  |
| --- |
| 355 |
| (9.1%) |

 | 0.96(0.79-1.18) |  |
| Antidepressants (2nd Quartile) |

|  |
| --- |
| 23 |
|  (8.9%) |

 |

|  |
| --- |
| 87 |
| (8.8%) |

 | 1.35(0.87-2.10) |  |

|  |
| --- |
| 128 |
| (9.7%) |

 |

|  |
| --- |
| 376 |
| (9.6%) |

 | **1.22(1.02-1.47)** |  |
| Antidepressants (3rd Quartile) |

|  |
| --- |
| 29 |
|  (11.3%) |

 |

|  |
| --- |
| 68 |
| (6.9%) |

 | **1.69(1.13-2.51)** |  |

|  |
| --- |
| 104 |
| (7.9%) |

 |

|  |
| --- |
| 372 |
| (9.5%) |

 | 0.89(0.73-1.09) |  |
| Antidepressants (4th Quartile) |

|  |
| --- |
| 35 |
|  (13.6%) |

 |

|  |
| --- |
| 67 |
| (6.8%) |

 | **2.17(1.50-3.14)** |  |

|  |
| --- |
| 118 |
| (8.9%) |

 |

|  |
| --- |
| 348 |
| (8.9%) |

 | 1.02(0.84-1.24) |  |
| Antiparkinsonian drugs (No use)\* |

|  |
| --- |
| 237 |
|  (92.5%) |

 |

|  |
| --- |
| 900 |
| (91.8%) |

 | 1.0 |  |

|  |
| --- |
| 1255 |
| (95.6%) |

 |

|  |
| --- |
| 3708 |
| (95.4%) |

 | 1.0 |  |
| Antiparkinsonian drugs (1stQuartile) |

|  |
| --- |
| 4 |
|  (1.5%) |

 |

|  |
| --- |
| 22 |
| (2.2%) |

 | 0.89(0.30-2.17) |  |

|  |
| --- |
| 11 |
| (0.8%) |

 |

|  |
| --- |
| 38 |
| (0.9%) |

 | 0.97(0.53-1.76) |  |
| Antiparkinsonian drugs (2nd Quartile) |

|  |
| --- |
| 0 |
|  (0.0%) |

 |

|  |
| --- |
| 12 |
| (1.2%) |

 |  |  |

|  |
| --- |
| 10 |
| (0.7%) |

 |

|  |
| --- |
| 45 |
| (1.1%) |

 | 0.78(0.42-1.46) |  |
| Antiparkinsonian drugs (3rd Quartile) |

|  |
| --- |
| 5 |
|  (1.9%) |

 |

|  |
| --- |
| 17 |
| (1.7%) |

 | 0.99(0.41-2.41) |  |

|  |
| --- |
| 13 |
| (0.9%) |

 |

|  |
| --- |
| 46 |
| (1.1%) |

 | 0.91(0.53-1.58) |  |
| Antiparkinsonian drugs (4th Quartile) |

|  |
| --- |
| 10 |
|  (3.9%) |

 |

|  |
| --- |
| 29 |
| (2.9%) |

 | 1.44(0.76-2.71) |  |

|  |
| --- |
| 23 |
| (1.7%) |

 |

|  |
| --- |
| 46 |
| (1.1%) |

 | 1.50(0.99-2.27) |  |
| Benzodiazepines (No use)\* |

|  |
| --- |
| 183 |
|  (71.4%) |

 |

|  |
| --- |
| 727 |
| (74.1%) |

 | 1.0 |  |

|  |
| --- |
| 986 |
| (75.1%) |

 |

|  |
| --- |
| 2828 |
| (72.8%) |

 | 1.0 |  |
| Benzodiazepines (1stQuartile) |

|  |
| --- |
| 19 |
|  (7.4%) |

 |

|  |
| --- |
| 75 |
| (7.6%) |

 | 1.12(0.70-1.80) |  |

|  |
| --- |
| 83 |
| (6.3%) |

 |

|  |
| --- |
| 265 |
| (6.8%) |

 | 1.00(0.801-1.25) |  |
| Benzodiazepines (2nd Quartile) |

|  |
| --- |
| 20 |
|  (7.8%) |

 |

|  |
| --- |
| 61 |
| (6.2%) |

 | 1.30(0.82-2.07) |  |

|  |
| --- |
| 82 |
| (6.2%) |

 |

|  |
| --- |
| 280 |
| (7.2%) |

 | 1.07(0.85-1.34) |  |
| Benzodiazepines (3rd Quartile) |

|  |
| --- |
| 22 |
|  (8.5%) |

 |

|  |
| --- |
| 55 |
| (5.6%) |

 | 1.39(0.89-2.17) |  |

|  |
| --- |
| 91 |
| (6.9%) |

 |

|  |
| --- |
| 251 |
| (6.4%) |

 | 1.14(0.92-1.42) |  |
| Benzodiazepines (4th Quartile) |

|  |
| --- |
| 12 |
|  (4.6%) |

 |

|  |
| --- |
| 62 |
| (6.3%) |

 | 0.80(0.44-1.43) |  |

|  |
| --- |
| 70 |
| (5.3%) |

 |

|  |
| --- |
| 259 |
| (6.6%) |

 | 1.01(0.79-1.28) |  |
| Z-Drugs (No use)\* |

|  |
| --- |
| 228 |
|  (89.0%) |

 |

|  |
| --- |
| 846 |
| (86.3%) |

 | 1.0 |  |

|  |
| --- |
| 1161 |
| (88.4%) |

 |

|  |
| --- |
| 3293 |
| (84.8%) |

 | 1.0 |  |
| Z-Drugs (1stQuartile) |

|  |
| --- |
| 12 |
|  (4.6%) |

 |

|  |
| --- |
| 35 |
| (3.5%) |

 | 1.29(0.72-2.32) |  |

|  |
| --- |
| 38 |
| (2.9%) |

 |

|  |
| --- |
| 165 |
| (4.2%) |

 | 0.84(0.61-1.17) |  |
| Z-Drugs (2nd Quartile) |

|  |
| --- |
| 5 |
|  (1.9%) |

 |

|  |
| --- |
| 29 |
| (2.9%) |

 | 0.7(0.30-1.81) |  |

|  |
| --- |
| 40 |
| (3.0%) |

 |

|  |
| --- |
| 137 |
| (3.5%) |

 | 0.86(0.63-1.18) |  |
| Z-Drugs (3rd Quartile) |

|  |
| --- |
| 5 |
|  (1.9%) |

 |

|  |
| --- |
| 34 |
| (3.4%) |

 | 0.57(0.23-1.39) |  |

|  |
| --- |
| 29 |
| (2.2%) |

 |

|  |
| --- |
| 147 |
| (3.7%) |

 | 0.79(0.54-1.14) |  |
| Z-Drugs (4th Quartile) |

|  |
| --- |
| 6 |
|  (2.3%) |

 |

|  |
| --- |
| 36 |
| (3.6%) |

 | 0.70(0.31-1.57) |  |

|  |
| --- |
| 44 |
| (3.3%) |

 |

|  |
| --- |
| 141 |
| (3.6%) |

 | 1.02(0.75-1.37) |  |
| Lithium (No use)\* |

|  |
| --- |
| 248 |
|  (96.8%) |

 |

|  |
| --- |
| 954 |
| (97.3%) |

 | 1.0 |  |

|  |
| --- |
| 1279 |
| (97.4%) |

 |

|  |
| --- |
| 3780 |
| (97.3%) |

 | 1.0 |  |
| Lithium (1stQuartile) |

|  |
| --- |
| 1 |
|  (0.3%) |

 |

|  |
| --- |
| 6 |
| (0.6%) |

 | 0.87(0.12-6.23) |  |

|  |
| --- |
| 3 |
| (0.2%) |

 |

|  |
| --- |
| 29 |
| (0.7%) |

 | 0.32(0.10-1.02) |  |
| Lithium (2nd Quartile) |

|  |
| --- |
| 3 |
|  (1.1%) |

 |

|  |
| --- |
| 7 |
| (0.7%) |

 | 1.96(0.62-6.12) |  |

|  |
| --- |
| 7 |
| (0.5%) |

 |

|  |
| --- |
| 26 |
| (0.6%) |

 | 0.90(0.43-1.90) |  |
| Lithium (3rd Quartile) |

|  |
| --- |
| 3 |
|  (1.1%) |

 |

|  |
| --- |
| 6 |
| (0.6%) |

 | 1.68(0.53-5.26) |  |

|  |
| --- |
| 15 |
| (1.1%) |

 |

|  |
| --- |
| 22 |
| (0.5%) |

 | **2.04(1.23-3.40)** |  |
| Lithium (4th Quartile) |

|  |
| --- |
| 1 |
|  (0.3%) |

 |

|  |
| --- |
| 7 |
| (0.7%) |

 | 0.60(0.08-4.32) |  |

|  |
| --- |
| 8 |
| (0.6%) |

 |

|  |
| --- |
| 26 |
| (0.6%) |

 | 0.77(0.38-1.54) |  |
| Mood stabilizers (No use)\* |

|  |
| --- |
| 231 |
|  (90.2%) |

 |

|  |
| --- |
| 880 |
| (89.8%) |

 | 1.0 |  |

|  |
| --- |
| 1224 |
| (93.2%) |

 |

|  |
| --- |
| 3524 |
| (90.7%) |

 | 1.0 |  |
| Mood stabilizers (1stQuartile) |

|  |
| --- |
| 2 |
|  (0.7%) |

 |

|  |
| --- |
| 24 |
| (2.4%) |

 | 0.34(0.08-1.37) |  |

|  |
| --- |
| 16 |
| (1.2%) |

 |

|  |
| --- |
| 89 |
| (2.2%) |

 | 0.76(0.46-1.25) |  |
| Mood stabilizers (2nd Quartile) |

|  |
| --- |
| 13 |
|  (5.0%) |

 |

|  |
| --- |
| 27 |
| (2.7%) |

 | **1.86(1.06-3.25)** |  |

|  |
| --- |
| 15 |
| (1.1%) |

 |

|  |
| --- |
| 94 |
| (2.4%) |

 | **0.59(0.35-0.99)** |  |
| Mood stabilizers (3rd Quartile) |

|  |
| --- |
| 6 |
|  (2.3%) |

 |

|  |
| --- |
| 28 |
| (2.8%) |

 | 0.97(0.43-2.19) |  |

|  |
| --- |
| 30 |
| (2.2%) |

 |

|  |
| --- |
| 81 |
| (2.0%) |

 | 1.01(0.70-1.44) |  |
| Mood stabilizers (4th Quartile) |

|  |
| --- |
| 4 |
|  (1.5%) |

 |

|  |
| --- |
| 21 |
| (2.1%) |

 | 0.90(0.33-2.43) |  |

|  |
| --- |
| 27 |
| (2.0%) |

 |

|  |
| --- |
| 95 |
| (2.4%) |

 | 0.82(0.56-1.21) |  |
| Addiction pharmacotherapy (No use)\* |

|  |
| --- |
| 250 |
|  (97.6%) |

 |

|  |
| --- |
| 960 |
| (97.9%) |

 | 1.0 |  |

|  |
| --- |
| 1293 |
| (98.5%) |

 |

|  |
| --- |
| 3783 |
| (97.4%) |

 | 1.0 |  |
| Addiction pharmacotherapy (1stQuartile) |

|  |
| --- |
| 1 |
|  (0.3%) |

 |

|  |
| --- |
| 7 |
| (0.7%) |

 | 0.43(0.06-3.07) |  |

|  |
| --- |
| 1 |
| (0.1%) |

 |

|  |
| --- |
| 22 |
| (0.5%) |

 | 0.29(0.04-2.07) |  |
| Addiction pharmacotherapy (2nd Quartile) |

|  |
| --- |
| 2 |
|  (0.7%) |

 |

|  |
| --- |
| 4 |
| (0.4%) |

 | 2.03(0.50-8.17) |  |

|  |
| --- |
| 4 |
| (0.3%) |

 |

|  |
| --- |
| 25 |
| (0.6%) |

 | 0.83(0.31-2.23) |  |
| Addiction pharmacotherapy (3rd Quartile) |

|  |
| --- |
| 0 |
|  (0.0%) |

 |

|  |
| --- |
| 4 |
| (0.4%) |

 |  |  |

|  |
| --- |
| 8 |
| (0.6%) |

 |

|  |
| --- |
| 28 |
| (0.7%) |

 | 1.18(0.59-2.38) |  |
| Addiction pharmacotherapy (4th Quartile) |

|  |
| --- |
| 3 |
| (1.1%) |

 |

|  |
| --- |
| 5 |
| (0.5%) |

 | 1.81(0.58-5.66) |  |

|  |
| --- |
| 6 |
| (0.4%) |

 |

|  |
| --- |
| 25 |
| (0.6%) |

 | 1.09(0.49-2.45) |  |

\*Reference. Significant results are bolded

**Table 6s.** Sensitivity analyses comparing associations of covariates with Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) between events occurring in treatment episodes < median duration and events occurring ≥ median duration within the prevalent LAI and OAP cohorts.

|  |  |  |
| --- | --- | --- |
|  | LAI BAMM events (N=5,051) | OAP BAMM events (N=13,321) |
|  | < Median (N=2,521) N (%) | ≥ median (N=2,530) N (%) | Univariate OR (95% CI) | Multivariate OR (95% CI) | < Median (N=6,655) N (%) | ≥ median (N=6,666) N (%) | Univariate OR (95% CI) | Multivariate OR (95% CI) |
| **Sociodemographic and baseline variables**  |
| Male gender |

|  |
| --- |
| 1308 |
| (51.9%) |

 |

|  |
| --- |
| 1329 |
| (52.5%) |

 | 0.97(0.87-1.08) | 0.94(0.83-1.06) |

|  |
| --- |
| 3345 |
| (50.3%) |

 |

|  |
| --- |
| 3344 |
| (50.2%) |

 | 1.00(0.93-1.07) | 0.94(0.87-1.02) |
| Age <=30 |

|  |
| --- |
| 400 |
| (15.8%) |

 |

|  |
| --- |
| 262 |
| (10.4%) |

 | 1.21(0.97-1.52) | 1.09(0.83-1.42) |

|  |
| --- |
| 1722 |
| (25.9%) |

 |

|  |
| --- |
| 1323 |
| (19.8%) |

 | 1.00(0.94-1.20) | **0.85(0.73-0.98)** |
| Age 31-40 |

|  |
| --- |
| 588 |
| (23.3%) |

 |

|  |
| --- |
| 659 |
| (26.0%) |

 | **0.71(0.58-0.86)** | **0.73(0.58-0.92)** |

|  |
| --- |
| 1545 |
| (23.2%) |

 |

|  |
| --- |
| 1686 |
| (25.3%) |

 | **0.75(0.66-0.84)** | **0.70(0.61-0.80)** |
| Age 41-50 |

|  |
| --- |
| 706 |
| (28.0%) |

 |

|  |
| --- |
| 850 |
| (33.6%) |

 | **0.66(0.55-0.79)** | **0.72(0.58-0.89)** |

|  |
| --- |
| 1445 |
| (21.71 |

 |

|  |
| --- |
| 1802 |
| (27.1%) |

 | **0.65(0.58-0.74)** | **0.65(0.57-0.74)** |
| Age 51-60 |

|  |
| --- |
| 480 |
| (19.0%) |

 |

|  |
| --- |
| 482 |
| (19.0%) |

 | **0.79(0.64-0.97)** | 0.83(0.66-1.03) |

|  |
| --- |
| 1033 |
| (15.5%) |

 |

|  |
| --- |
| 1107 |
| (16.6%) |

 | **0.76(0.67-0.87)** | **0.75(0.65-0.86)** |
| Age >60\* |

|  |
| --- |
| 347 |
| (13.8%) |

 |

|  |
| --- |
| 277 |
| (10.9%) |

 |  |  |

|  |
| --- |
| 910 |
| (13.7%) |

 |

|  |
| --- |
| 748 |
| (11.2%) |

 |  |  |
| Illness duration <5 years |

|  |
| --- |
| 818 |
| (32.4%) |

 |

|  |
| --- |
| 602 |
| (23.8%) |

 | **1.55(1.35-1.77)** | 1.11(0.92-1.34) |

|  |
| --- |
| 3774 |
| (56.7%) |

 |

|  |
| --- |
| 2817 |
| (42.3%) |

 | **1.69(1.54-1.81)** | **1.25(1.10-1.42)** |
| Illness duration 5-15 years |

|  |
| --- |
| 685 |
| (27.2%) |

 |

|  |
| --- |
| 767 |
| (30.3%) |

 | 1.02(0.89-1.16) | 1.01(0.86-1.18) |

|  |
| --- |
| 1201 |
| (18.0%) |

 |

|  |
| --- |
| 1756 |
| (26.3%) |

 | 0.85(0.77-0.93) | 1.01(0.89-1.11) |
| Illness duration >15 years\* |

|  |
| --- |
| 1018 |
| (40.4%) |

 |

|  |
| --- |
| 1161 |
| (45.9%) |

 |  |  |

|  |
| --- |
| 1680 |
| (25.2%) |

 |

|  |
| --- |
| 2093 |
| (31.4%) |

 |  |  |
| 0-3 previous hospitalizations\*  |

|  |
| --- |
| 418 |
| (16.6%) |

 |

|  |
| --- |
| 531 |
| (21.0%) |

 |  |  |

|  |
| --- |
| 2687 |
| (40.4%) |

 |

|  |
| --- |
| 3153 |
| (47.3%) |

 |  |  |
| 4-6 previous hospitalizations  |

|  |
| --- |
| 470 |
| (18.6%) |

 |

|  |
| --- |
| 639 |
| (25.3%) |

 | 0.93(0.78-1.11) | 0.94(0.77-1.14) |

|  |
| --- |
| 1458 |
| (21.9%) |

 |

|  |
| --- |
| 1646 |
| (24.7%) |

 | 1.03(0.95-1.13) | **1.20(1.09-1.32)** |
| >6 previous hospitalizations |

|  |
| --- |
| 1633 |
| (64.8%) |

 |

|  |
| --- |
| 1360 |
| (53.7%) |

 | **1.52(1.31-1.76)** | **1.51(1.26-1.82)** |

|  |
| --- |
| 2510 |
| (37.7%) |

 |

|  |
| --- |
| 1867 |
| (28.0%) |

 | **1.57(1.45-1.70)** | **1.93(1.74-2.14)** |
| Last hospital discharge <2 months |

|  |
| --- |
| 1906 |
| (75.6%) |

 |

|  |
| --- |
| 1127 |
| (44.5%) |

 | **5.3(4.66-6.22)** | **4.39(3.73-5.15)** |

|  |
| --- |
| 4548 |
| (68.3%) |

 |

|  |
| --- |
| 2791 |
| (41.8%) |

 | **4.06(3.75-4.41)** | **3.24(2.93-3.59)** |
| Last hospital discharge 2-12 months |

|  |
| --- |
| 284 |
| (11.3%) |

 |

|  |
| --- |
| 348 |
| (13.7%) |

 | **2.60(2.13-3.17)** | **2.14(1.74-2.63)** |

|  |
| --- |
| 855 |
| (12.8%) |

 |

|  |
| --- |
| 749 |
| (11.2%) |

 | **2.85(2.53-3.20)** | **2.32(2.05-2.63)** |
| Last hospital discharge <12 months\* |

|  |
| --- |
| 331 |
| (13.1%) |

 |

|  |
| --- |
| 1055 |
| (41.7%) |

 |  |  |

|  |
| --- |
| 1252 |
| (18.8%) |

 |

|  |
| --- |
| 3126 |
| (46.9%) |

 |  |  |
| **Comorbidities diagnosed before treatment episode** |
| Substance use disorders |

|  |
| --- |
| 472 |
| (18.7%) |

 |

|  |
| --- |
| 295 |
| (11.7%) |

 | **1.74(1.49-2.04)** | **1.38(1.16-1.65)** |

|  |
| --- |
| 966 |
| (14.5%) |

 |

|  |
| --- |
| 620 |
| (9.3%) |

 | **1.65(1.48-1.84)** | **1.33(1.18-1.49)** |
| Suicidality |

|  |
| --- |
| 89 |
| (3.5%) |

 |

|  |
| --- |
| 106 |
| (4.2%) |

 | 0.83(0.62-1.11) |  |

|  |
| --- |
| 189 |
| (2.8%) |

 |

|  |
| --- |
| 191 |
| (2.8%) |

 | 0.99(0.80-1.21) |  |
| Cancer |

|  |
| --- |
| 51 |
| (2.0%) |

 |

|  |
| --- |
| 51 |
| (2.0%) |

 | 1.01(0.67-1.48) |  |

|  |
| --- |
| 145 |
| (2.1%) |

 |

|  |
| --- |
| 129 |
| (1.9%) |

 | 1.12(0.88-1.43) |  |
| Cardiovascular disease |

|  |
| --- |
| 319 |
| (12.7%) |

 |

|  |
| --- |
| 209 |
| (8.3%) |

 | **1.60(1.33-1.93)** | **1.39(1.13-1.71)** |

|  |
| --- |
| 795 |
| (11.9%) |

 |

|  |
| --- |
| 611 |
| (9.1%) |

 | **1.34(1.20-1.50)** | **1.22(1.08-1.38)** |
| Intellectual disability |

|  |
| --- |
| 150 |
| (5.9%) |

 |

|  |
| --- |
| 148 |
| (5.8%) |

 | 1.01(0.80-1.28) |  |

|  |
| --- |
| 317 |
| (4.7%) |

 |

|  |
| --- |
| 305 |
| (4.5%) |

 | 1.04(0.88-1.22) |  |
| Cognitive disorders |

|  |
| --- |
| 6 |
| (0.2%) |

 |

|  |
| --- |
| 3 |
| (0.1%) |

 | 2.00(0.50-8.04) |  |

|  |
| --- |
| 23 |
| (0.3%) |

 |

|  |
| --- |
| 12 |
| (0.1%) |

 | 1.92(0.95-3.86) |  |
| Tardive dyskinesia |

|  |
| --- |
| 3 |
| (0.1%) |

 |

|  |
| --- |
| 0 |
| (0.0%) |

 |  |  |

|  |
| --- |
| 1 |
| (0.1%) |

 |

|  |
| --- |
| 2 |
| (0.1%) |

 | 0.50(0.04-5.52) |  |
| Diabetes |

|  |
| --- |
| 136 |
| (5.3%) |

 |

|  |
| --- |
| 67 |
| (2.7%) |

 | **2.09(1.55-2.82)** | **1.85(1.33-2.57)** |

|  |
| --- |
| 226 |
| (3.4%) |

 |

|  |
| --- |
| 184 |
| (2.7%) |

 | **1.23(1.01-1.50)** | 1.14(0.92-1.42) |
| Asthma |

|  |
| --- |
| 81 |
| (3.2%) |

 |

|  |
| --- |
| 49 |
| (1.9%) |

 | **1.68(1.17-2.40)** | 1.38(0.94-2.04) |

|  |
| --- |
| 198 |
| (2.9%) |

 |

|  |
| --- |
| 114 |
| (1.7%) |

 | **1.76(1.39-2.22)** | **1.29(1.01-1.64)** |
| **Co-treatment at baseline** |
| Antidepressants  |

|  |
| --- |
| 517 |
| (20.5%) |

 |

|  |
| --- |
| 330 |
| (13.0%) |

 | **1.72(1.47-2**.**00)** | **1.43(1.21-1.69)** |

|  |
| --- |
| 1884 |
| (28.3%) |

 |

|  |
| --- |
| 1440 |
| (21.6%) |

 | **1.43(1.32-1.55)** | **1.21(1.11-1.32)** |
| Benzodiazepines  |

|  |
| --- |
| 804 |
| (31.9%) |

 |

|  |
| --- |
| 651 |
| (25.7%) |

 | **1.35(1.19-1.52)** | 1.14(0.99-1.31) |

|  |
| --- |
| 2144 |
| (32.2%) |

 |

|  |
| --- |
| 1913 |
| (28.7%) |

 | **1.18(1.09-1.27)** | 1.03(0.95-1.12) |
| z-drugs  |

|  |
| --- |
| 214 |
| (8.4%) |

 |

|  |
| --- |
| 167 |
| (6.6%) |

 | **1.31(1.06-1.62)** | 1.04(0.83-1.31) |

|  |
| --- |
| 615 |
| (9.2%) |

 |

|  |
| --- |
| 434 |
| (6.5%) |

 | **1.46(1.28-1.66)** | **1.22(1.06-1.40)** |
| Antiparkinsonian drugs  |

|  |
| --- |
| 452 |
| (17.9%) |

 |

|  |
| --- |
| 529 |
| (20.9%) |

 | **0.82(0.71-0.95)** | 0.86(0.74-1.01) |

|  |
| --- |
| 663 |
| (9.9%) |

 |

|  |
| --- |
| 785 |
| (11.7%) |

 | 0.82(0.74-0.92) | **0.86(0.76-0.97)** |
| Lithium  |

|  |
| --- |
| 149 |
| (5.9%) |

 |

|  |
| --- |
| 149 |
| (5.9%) |

 | 1.01(0.79-1.26) |  |

|  |
| --- |
| 463 |
| (6.9%) |

 |

|  |
| --- |
| 441 |
| (6.6%) |

 | 1.05(0.92-1.20) |  |
| Mood stabilizers |

|  |
| --- |
| 319 |
| (12.6%) |

 |

|  |
| --- |
| 246 |
| (9.7%) |

 | **1.34(1.12-1.60)** | 0.96(0.79-1.17) |

|  |
| --- |
| 853 |
| (12.8%) |

 |

|  |
| --- |
| 639 |
| (9.5%) |

 | **1.38(1.24-1.54)** | 1.06(0.94-1.19) |
| Addiction pharmacotherapy |

|  |
| --- |
| 2 |
| (0.1%) |

 |

|  |
| --- |
| 0 |
| (0.0%) |

 |  |  |

|  |
| --- |
| 63 |
| (0.9%) |

 |

|  |
| --- |
| 36 |
| (0.5%) |

 | **1.76(1.16-2.65)** | 1.01(0.65-1.52) |

\*Reference. Significant results are bolded

**Table 7s.** Proportion of Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) and time to event in days by time since last hospitalization at treatment onset

|  |  |  |
| --- | --- | --- |
|  | BAMM events in the prevalent cohort | BAMM events in the incident cohort |
|  | LAI (N=5,051) | OAP (N=13,321) | LAI (N=385) | OAP (N=1,439) |
|  | N (%) | Median time to event, (IQR) | N (%) | Median time to event, (IQR) | N (%) | Median time to event, (IQR) | N (%) | Median time to event, (IQR) |
|  0-2 months | 3033(60.0%) | 190(99-484) | 7339(55.0%) | 228(113-589) | 338(87.7%) | 190.5(104-569) | 1202(83.5%) | 257.5(119-720) |
|  2-12 months | 632(12.5%) | 340(143-838.5) | 1604(12.0%) | 300(141-765) | 28(7.2%) | 233(134-670) | 165(11.4%) | 253(128-715) |
|  >12 months | 1386(27.4%) | 780(309-1726) | 4378(32.8%) | 775(295-1879) | 19(4.9%) | 210(131-431) | 72(5.0%) | 288(131-858.5) |

**Table 8s.** Association between baseline characteristics in the prevalent cohort with a previous Breakthrough Psychosis on Antipsychotic Maintenance (BAMM) episode and a second BAMM event in the prevalent cohort

|  |  |  |
| --- | --- | --- |
|  | LAI (N=1,748) | OAP (N=9,953) |
| Variable | BAMM (N,%)N=387 | NO BAMM (N,%) N=1,361 | Univariate HR (95% CI) | Multivariate HR (95% CI) | BAMM (N,%)N=5,225 | NO BAMM (N,%)N=4,728 | Univariate HR (95% CI) | Multivariate HR (95% CI) |
| **Sociodemographic variables** |
| Male Gender |

|  |
| --- |
| 1080 |
| (52.4%) |

 |

|  |
| --- |
| 1120 |
| (51.6%) |

 | 1.01(0.93-1.10) | 0.98(0.89-1.07) |

|  |
| --- |
| 2612 |
| (49.9%) |

 |

|  |
| --- |
| 2307 |
| (48.7%) |

 | 1.01(0.96-1.07) | 0.97(0.92-1.03) |
| Age <=30 |

|  |
| --- |
| 194 |
| (9.4%) |

 |

|  |
| --- |
| 212 |
| (9.7%) |

 | **1.49(1.24-1.80)** | **1.57(1.29-1.90)** |

|  |
| --- |
| 981 |
| (18.7%) |

 |

|  |
| --- |
| 746 |
| (15.7%) |

 | **1.44(1.31-1.59)** | **1.57(1.41-1.73)** |
| Age 31-40 |

|  |
| --- |
| 450 |
| (21.8%) |

 |

|  |
| --- |
| 418 |
| (19.2%) |

 | **1.37(1.18-1.60)** | **1.34(1.14-1.57)** |

|  |
| --- |
| 1281 |
| (24.5%) |

 |

|  |
| --- |
| 903 |
| (19.1%) |

 | **1.36(1.24-1.49)** | **1.34(1.22-1.484)** |
| Age 41-50 |

|  |
| --- |
| 700 |
| (33.9%) |

 |

|  |
| --- |
| 605 |
| (27.8%) |

 | **1.26(1.09-1.45)** | **1.16(1.01-1.35)** |

|  |
| --- |
| 1337 |
| (25.5%) |

 |

|  |
| --- |
| 1053 |
| (22.2%) |

 | **1.22(1.11-1.34)** | **1.14(1.04-1.25)** |
| Age 51-60 |

|  |
| --- |
| 451 |
| (21.8%) |

 |

|  |
| --- |
| 544 |
| (25.0%) |

 | 1.02(0.87-1.18) | 0.97(0.83-1.13) |

|  |
| --- |
| 947 |
| (18.1%) |

 |

|  |
| --- |
| 1002 |
| (21.2%) |

 | 1.09(0.99-1.21) | 1.02(0.92-1.13) |
| Age >60\* |

|  |
| --- |
| 265 |
| (12.8%) |

 |

|  |
| --- |
| 391 |
| (18.0%) |

 | 1.0 | 1.01 |

|  |
| --- |
| 679 |
| (13.0%) |

 |

|  |
| --- |
| 1024 |
| (21.6%) |

 | 1.01 | 1.01 |
| **Comorbidity at baseline**  |
| Substance use disorders |

|  |
| --- |
| 339 |
| (16.4%) |

 |

|  |
| --- |
| 376 |
| (17.3%) |

 | 1.11(0.99-1.25) |  |

|  |
| --- |
| 645 |
| (12.3%) |

 |

|  |
| --- |
| 667 |
| (14.1%) |

 | 1.08(0.99-1.17) |  |
| Suicidality |

|  |
| --- |
| 96 |
| (4.6%) |

 |

|  |
| --- |
| 73 |
| (3.3%) |

 | 1.09(0.89-1.34) | 1.00(0.81-1.23) |

|  |
| --- |
| 176 |
| (3.3%) |

 |

|  |
| --- |
| 105 |
| (2.2%) |

 | **1.38(1.18-1.60)** | **1.24(1.06-1.44)** |
| Cancer |

|  |
| --- |
| 43 |
| (2.0%) |

 |

|  |
| --- |
| 53 |
| (2.4%) |

 | 1.09(0.80-1.47) |  |

|  |
| --- |
| 105 |
| (2.0%) |

 |

|  |
| --- |
| 137 |
| (2.9%) |

 | 0.90(0.74-1.10) |  |
| Cardiovascular disease |

|  |
| --- |
| 196 |
| (9.5%) |

 |

|  |
| --- |
| 283 |
| (13.0%) |

 | 0.87(0.75-1.01) |  |

|  |
| --- |
| 534 |
| (10.2%) |

 |

|  |
| --- |
| 683 |
| (14.4%) |

 | 0.91(0.83-1.00) |  |
| Intellectual disability |

|  |
| --- |
| 134 |
| (6.5%) |

 |

|  |
| --- |
| 132 |
| (6.0%) |

 | 0.97(0.81-1.15) |  |

|  |
| --- |
| 250 |
| (4.7%) |

 |

|  |
| --- |
| 254 |
| (5.3%) |

 | 0.90(0.79-1.02) |  |
| Cognitive disorders |

|  |
| --- |
| 6 |
| (0.2%) |

 |

|  |
| --- |
| 9 |
| (0.4%) |

 | 0.92(0.41-2.05) |  |

|  |
| --- |
| 25 |
| (0.4%) |

 |

|  |
| --- |
| 41 |
| (0.8%) |

 | 1.06(0.71-1.57) |  |
| Tardive dyskinesia |

|  |
| --- |
| 0 |
| (0.0%) |

 |

|  |
| --- |
| 1 |
| (0.1%) |

 |  |  |

|  |
| --- |
| 1 |
| (0.1%) |

 |

|  |
| --- |
| 4 |
| (0.1%) |

 | 0.53(0.07-3.75) |  |
| Diabetes |

|  |
| --- |
| 85 |
| (4.1%) |

 |

|  |
| --- |
| 110 |
| (5.0%) |

 | **1.05(0.84-1.30)** | **1.10(0.88-1.37)** |

|  |
| --- |
| 139 |
| (2.6%) |

 |

|  |
| --- |
| 240 |
| (5.0%) |

 | **0.80(0.68-0.95)** | 0.87(0.73-1.03) |
| Asthma |

|  |
| --- |
| 58 |
| (2.8%) |

 |

|  |
| --- |
| 61 |
| (2.8%) |

 | 1.07(0.82-1.39) |  |

|  |
| --- |
| 121 |
| (2.3%) |

 |

|  |
| --- |
| 122 |
| (2.5%) |

 | 1.13(0.94-1.36) |  |
| **Illness characteristics** |
| Disease duration <=5 years |

|  |
| --- |
| 396 |
| (19.2%) |

 |

|  |
| --- |
| 486 |
| (22.0%) |

 | 1.03(0.92-1.16) |  |

|  |
| --- |
| 2143 |
| (41.0%) |

 |

|  |
| --- |
| 2058 |
| (43.5%) |

 | 1.07(1.01-1.14) |  |
| Disease duration 5-15 years |

|  |
| --- |
| 581 |
| (28.2%) |

 |

|  |
| --- |
| 597 |
| (27.5%) |

 | 1.02(0.93-1.13) |  |

|  |
| --- |
| 1255 |
| (24.0%) |

 |

|  |
| --- |
| 1051 |
| (22.2%) |

 | 1.04(0.96-1.11) |  |
| Disease duration >15 years\* |

|  |
| --- |
| 1083 |
| (52.5%) |

 |

|  |
| --- |
| 1087 |
| (50.0%) |

 | 1.0 |  |

|  |
| --- |
| 1827 |
| (34.9%) |

 |

|  |
| --- |
| 1619 |
| (34.2%) |

 | 1.0 |  |
| Schizophrenia |

|  |
| --- |
| 1699 |
| (82.4%) |

 |

|  |
| --- |
| 1776 |
| (81.8%) |

 | 1.16(0.89-1.49) | 1.14(0.88-1.47) |

|  |
| --- |
| 3868 |
| (74.0%) |

 |

|  |
| --- |
| 3437 |
| (72.6%) |

 | **1.24(1.10-1.40)** | **1.19(1.05-1.34)** |
| Schizoaffective disorder |

|  |
| --- |
| 300 |
| (14.5%) |

 |

|  |
| --- |
| 309 |
| (14.2%) |

 | 1.22(0.93-1.61) | 1.12(0.84-1.49) |

|  |
| --- |
| 1062 |
| (20.3%) |

 |

|  |
| --- |
| 917 |
| (19.4%) |

 | **1.30(1.15-1.48)** | **1.21(1.06-1.38)** |
| Other psychoses\* |

|  |
| --- |
| 61 |
| (2.9%) |

 |

|  |
| --- |
| 85 |
| (3.9%) |

 | 1.0 | 1.0 |

|  |
| --- |
| 295 |
| (5.6%) |

 |

|  |
| --- |
| 374 |
| (7.9%) |

 | 1.0 | 1.0 |
| **Treatment history characteristics upon initiation of treatment episode** |
| 0-3 previous hospitalizations\*  |

|  |
| --- |
| 129 |
| (6.2%) |

 |

|  |
| --- |
| 230 |
| (10.6%) |

 | 1.0 | 1.0 |

|  |
| --- |
| 1210 |
| (23.1%) |

 |

|  |
| --- |
| 1491 |
| 31.5%) |

 | 1.0 | 1.0 |
| 4-6 previous hospitalizations  |

|  |
| --- |
| 340 |
| (16.5%) |

 |

|  |
| --- |
| 516 |
| (23.7%) |

 | 1.15(0.94-1.41) | 1.15(0.94-1.41) |

|  |
| --- |
| 1609 |
| (30.7%) |

 |

|  |
| --- |
| 1582 |
| (33.4%) |

 | **1.17(1.08-1.26)** | **1.19(1.10-1.28)** |
| >6 previous hospitalizations |

|  |
| --- |
| 1591 |
| (77.2%) |

 |

|  |
| --- |
| 1424 |
| (65.6%) |

 | **1.78(1.49-2.13)** | **1.78(1.48-2.14)** |

|  |
| --- |
| 2406 |
| (46.0%) |

 |

|  |
| --- |
| 1655 |
| (35.0%) |

 | **1.69(1.58-1.81)** | **1.75(1.63-1.88)** |
| Time since hospital discharge <2 months |

|  |
| --- |
| 2030 |
| (98.5%) |

 |

|  |
| --- |
| 2102 |
| (96.8%) |

 | **3.6(1.37-9.76)** | **3.32(1.24-8.88)** |

|  |
| --- |
| 4960 |
| (94.9%) |

 |

|  |
| --- |
| 4269 |
| (90.2%) |

 | **1.81(1.47-2.24)** | **1.82(1.47-2.25)** |
| Time since hospital discharge 2-12 months |

|  |
| --- |
| 26 |
| (1.2%) |

 |

|  |
| --- |
| 46 |
| (2.1%) |

 | 1.15(0.94-1.41) | 1.15(0.94-1.41) |

|  |
| --- |
| 178 |
| (3.4%) |

 |

|  |
| --- |
| 251 |
| (5.3%) |

 | **1.17(1.08-1.26)** | **1.19(1.10-1.28)** |
| Time since hospital discharge <12 months\* |

|  |
| --- |
| 4 |
| (0.2%) |

 |

|  |
| --- |
| 22 |
| (1.0%) |

 | 1.0 | 1.0 |

|  |
| --- |
| 87 |
| (1.6%) |

 |

|  |
| --- |
| 208 |
| (4.4%) |

 | 1.0 | 1.0 |
| **Co-treatment at baseline** |
| Antidepressants  |

|  |
| --- |
| 394 |
| (19.1%) |

 |

|  |
| --- |
| 388 |
| (17.8%) |

 | **1.12(1.01-1.25)** | 1.07(0.95-1.19) |

|  |
| --- |
| 1484 |
| (28.4%) |

 |

|  |
| --- |
| 1379 |
| (29.1%) |

 | 1.00(0.94-1.06) | 0.99(0.93-1.05) |
| Benzodiazepines  |

|  |
| --- |
| 656 |
| (31.8%) |

 |

|  |
| --- |
| 637 |
| (29.3%) |

 | **1.15(1.05-1.26)** | 1.09(0.99-1.20) |

|  |
| --- |
| 1861 |
| (35.6%) |

 |

|  |
| --- |
| 1615 |
| (34.1%) |

 | **1.10(1.04-1.16)** | **1.08(1.01-1.14)** |
| Z-drugs  |

|  |
| --- |
| 183 |
| (8.8%) |

 |

|  |
| --- |
| 172 |
| (7.9%) |

 | 1.15(0.98-1.33) |  |

|  |
| --- |
| 435 |
| (8.3%) |

 |

|  |
| --- |
| 479 |
| (10.1%) |

 | 0.93(0.84-1.02) |  |
| Antiparkinsonian drugs  |

|  |
| --- |
| 426 |
| (20.6%) |

 |

|  |
| --- |
| 384 |
| (17.7%) |

 | **1.13(1.01-1.26)** | **1.11(1.00-1.24)** |

|  |
| --- |
| 496 |
| (9.4%) |

 |

|  |
| --- |
| 423 |
| (8.9%) |

 | 1.08(0.99-1.19) | 1.07(0.97-1.18) |
| Lithium  |

|  |
| --- |
| 135 |
| (6.5%) |

 |

|  |
| --- |
| 122 |
| (5.6%) |

 | 1.12(0.94-1.33) | 1.07(0.88-1.29) |

|  |
| --- |
| 424 |
| (8.1%) |

 |

|  |
| --- |
| 311 |
| (6.5%) |

 | **1.14(1.03-1.25)** | 1.02(0.91-1.13) |
| Mood stabilizers |

|  |
| --- |
| 277 |
| (12.7%) |

 |

|  |
| --- |
| 303 |
| (14.7%) |

 | **1.18(1.05-1.343)** | 1.09(0.96-1.24) |

|  |
| --- |
| 805 |
| (15.4%) |

 |

|  |
| --- |
| 664 |
| (14.0%) |

 | **1.13(1.05-1.22)** | 1.04(0.96-1.13) |
| Addiction pharmacotherapy  |

|  |
| --- |
| 29 |
| (1.4%) |

 |

|  |
| --- |
| 26 |
| (1.2%) |

 | **1.46(1.01-2.10)** | 1.38(0.95-2.00) |

|  |
| --- |
| 71 |
| (1.3%) |

 |

|  |
| --- |
| 49 |
| (1.0%) |

 | 1.16(0.92-1.47) | 1.08(0.85-1.37) |

\*Reference. Significant results are bolded