**Supplementary material**

**Figure S1. Antipsychotic medication exposure during year two to five and definition of AP1-4**

**Figure S2. Comparison of AP1-4 in main analyses (ap status) and in sensitivity analyses (conservative ap status, half DDD ap status, admissions ap status, and latest half ap status)**

**Table S1. Baseline characteristics of the study population at year 2**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Baseline characteristics year 2** | AP 1 (Continuous AP)  n=1985 | AP 2 (Sustained discontinuation)  n=721 | AP 3 (Non-sustained discontinuation)  n=10394 | AP 4 (No AP)  n=8251 | Total  N=21351 | Lost to follow-up (year 2-5)  N=1917d |
| Count (column%) | Count (column%) | Count (column%) | Count (column%) | Count (column%) | Count (column%) |
| Sex (female) | 876(44.1) | 321(44.5) | 4815(46.3) | 3524(42.7) | 9536(44.7)\*\*\* | 628(32.8) |
| Age at diagnosis (median (25%-75%)) | 35.1(26.4-45.1) | 32.5(24.1-43.1) | 31.3(23.8-42.0) | 31.4(23.5-43.7) | 31.7(23.9-43.1)\*\*\* | 36.0(25.5-53.8) |
| Immigrants | 191(9.6) | 109(15.1) | 1464(14.1) | 1278(15.5) | 3042(14.2)\*\*\* | 375(19.6) |
| Other F2 diagnosis preceding schizophrenia | 1070(53.9) | 318(44.1) | 5056(48.6) | 2967(36.0) | 9411(44.1)\*\*\* | 907(47.3) |
| Diagnosing place (inpatient) | 982(49.5) | 327(45.4) | 4633(44.6) | 2379(28.8) | 8321(39.0)\*\*\* | 850(44.3) |
| Index hospitalization length (days) (median (25%-75%)) | 52(18-110) | 60(23-134) | 60(25-120) | 47(16-91) | 55(21-112)\*\*\* | 48(16-96) |
| Education (upper secondary school completed) a | 778(40.4) | 303(44.4) | 4519(45.1) | 3481(44.6) | 9081(44.5)\*\* | 558(37.6) |
| Employment (work or study)b | 127(6.4) | 66(9.2) | 1240(11.9) | 1692(20.5) | 3125(14.6)\*\*\* | 84(4.4) |
| Living with partnerc | 849(42.8) | 301(41.7) | 4370(42.1) | 3601(43.8) | 9121(42.8) | 674(40.0) |
| Living with childrenc | 223(11.2) | 95(13.2) | 1323(12.7) | 1275(15.5) | 2916(13.7)\*\*\* | 113(6.7) |
| **Measures of year 0-2** |  |  |  |  |  |  |
| No alcohol misuse | 1781(89.7) | 625(86.7) | 9409(90.5) | 7449(90.3) | 19264(90.2)\*\* | 1592(83.0) |
| No substance misuse | 1776(89.5) | 605(83.9) | 8843(85.1) | 6976(84.5) | 18200(85.2)\*\*\* | 1399(73.0) |

Note: Statistical tests for baseline differences between groups were performed. Chi-square tests were used for dichotomous variables and Kruskal Wallis tests were used for medians.

\*p value ≤ 0.05, \*\* p value ≤ 0.01 and \*\*\*p value ≤ 0.001

a 4.4% missing, b 0.1% missing, c 0.2% missing, d Missing in lost to follow-up variables education (22.6% missing), employment 0.2% missing, living with partner (12.0% missing) and living with children (12.0% missing)

**Table S2. Sensitivity analyses of employment year five to six using data from DREAM**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **DREAM database measured year 6** | AP 1 (Continuous AP)  n=1179 | AP 2 (Sustained discontinuation)  n=476 | | | AP 3 (Non-sustained discontinuation)  n=5935 | | | AP 4 (No AP)  n=4796 | | | Total  N=12386 |
| Employment (work or study) | Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
|  | 3.26 | 2.03-5.21 | 0.00 | 2.78 | 1.94-3.98 | 0.00 | 9.26 | 6.51-13.18 | 0.00 | 0.00 |

a Reference group. Abbreviations: OR=Odds ratio, CI=Confidence interval

**Table S3. Odds ratios of living situation, employment, alcohol and substance misuse, involuntary admissions, and coercion**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcomes measured year 6** | AP 1 (Continuous AP) a  n=1940 | AP 2 (Sustained discontinuation)  n=703 | | | AP 3 (Non-sustained discontinuation)  n=10124 | | | AP 4 (No AP)  n=8054 | | | Total  N=20821 |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
| Employment (work or study) b |  | 2.60 | 1.91-3.54 | 0.00 | 2.04 | 1.64-2.53 | 0.00 | 5.64 | 4.56-6.97 | 0.00 | 0.00 |
| Living with partner c |  | 1.01 | 0.85-1.21 | 0.89 | 0.96 | 0.87-1.07 | 0.46 | 1.14 | 1.031.27- | 0.01 | 0.00 |
| Living with children c |  | 1.98 | 1.53-2.56 | 0.00 | 1.25 | 1.05-1.48 | 0.01 | 2.00 | 1.69-2.38 | 0.00 | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  |  |
| No alcohol misuse |  | 1.22 | 0.85-1.75 | 0.29 | 0.99 | 0.82-1.19 | 0.90 | 1.40 | 1.141.71- | 0.00 | 0.00 |
| No substance misuse |  | 0.66 | 0.49-0.90 | 0.01 | 0.66 | 0.54-0.80 | 0.00 | 0.91 | 0.75-1.11 | 0.37 | 0.00 |
| No involuntary admissions |  | 0.49 | 0.33-0.73 | 0.00 | 0.54 | 0.42-0.71 | 0.00 | 0.84 | 0.64-1.11 | 0.23 | 0.00 |
| No coercion |  | 0.73 | 0.54-0.99 | 0.04 | 0.64 | 0.53-0.76 | 0.00 | 1.26 | 1.04-1.53 | 0.02 | 0.00 |

a Reference group. b 0.1% missing; c 1.0% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

**Table S4. Sensitivity analyses of odds ratios of living situation, employment, alcohol and substance misuse, involuntary admissions and coercion with conservative ap status, half DDD ap status, admissions ap status, latest half ap status, and other F2 diagnosis preceding schizophrenia ap status.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Conservative ap status** | | | | | | | | | | | |
| **outcomes measured year 6** | *AP 1 (Continuous AP)*a  *n=3937* | *AP 2 (Sustained discontinuation)*  *n=1331* | | | *AP 3 (Non-sustained discontinuation)*  *n=7628* | | | *AP 4 (No AP)*  *n=7925* | | | *Total*  *N=20821* |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
| Employment (work or study) b |  | 2.33 | 1.89-2.88 | 0.00 | 1.82 | 1.56-2.12 | 0.00 | 4.75 | 4.12-5.48 | 0.00 | 0.00 |
| Living with partner c |  | 1.04 | 0.92-1.18 | 0.55 | 1.02 | 0.94-1.11 | 0.58 | 1.20 | 1.11-1.30 | 0.00 | 0.00 |
| Living with children c |  | 1.96 | 1.63-2.36 | 0.00 | 1.27 | 1.11-1.44 | 0.00 | 2.00 | 1.69-2.38 | 0.00 | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  |  |
| No alcohol misuse |  | 1.04 | 0.82-1.34 | 0.73 | 0.98 | 0.84-1.14 | 0.81 | 1.39 | 1.19-1.63 | 0.00 | 0.00 |
| No substance misuse |  | 0.69 | 0.55-0.86 | 0.00 | 0.60 | 0.52-0.70 | 0.00 | 0.92 | 0.79-1.07 | 0.28 | 0.00 |
| No involuntary admissions |  | 0.62 | 0.46-0.82 | 0.00 | 0.54 | 0.45-0.66 | 0.00 | 0.93 | 0.76-1.14 | 0.47 | 0.00 |
| No coercion |  | 0.83 | 0.66-1.03 | 0.09 | 0.62 | 0.54-0.71 | 0.00 | 1.35 | 1.16-1.56 | 0.00 | 0.00 |

a Reference group. b 0.1%missing; c 1.0% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **half DDD ap status** | | | | | | | | | | | |
| **Outcomes measured year 6** | *AP 1 (Continuous AP)*a  *n=5127* | *AP 2 (Sustained discontinuation)*  *n=1102* | | | *AP 3 (Non-sustained discontinuation)*  *n=8089* | | | *AP 4 (No AP)*  *n=6503* | | | *Total N=20821* |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
| Employment (work or study) b |  | 2.61 | 2.13-3.20 | 0.00 | 1.92 | 1.68-2.19 | 0.00 | 4.94 | 4.35-5.62 | 0.00 | 0.00 |
| Living with partner c |  | 1.20 | 1.05-1.37 | 0.01 | 1.03 | 0.96-1.11 | 0.40 | 1.27 | 1.18-1.37 | 0.00 | 0.00 |
| Living with children c |  | 2.40 | 2.00-2.87 | 0.00 | 1.33 | 1.18-1.50 | 0.00 | 2.10 | 1.87-2.36 | 0.00 | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  |  |
| No alcohol misuse |  | 1.15 | 0.87-1.53 | 0.32 | 0.88 | 0.77-1.01 | 0.07 | 1.30 | 1.11-1.52 | 0.00 | 0.00 |
| No substance misuse |  | 0.92 | 0.72-1.17 | 0.49 | 0.64 | 0.56-0.73 | 0.00 | 0.99 | 0.86-1.15 | 0.92 | 0.00 |
| No involuntary admissions |  | 0.72 | 0.53-0.97 | 0.03 | 0.61 | 0.51-0.72 | 0.00 | 0.99 | 0.82-1.20 | 0.92 | 0.00 |
| No coercion |  | 0.90 | 0.71-1.13 | 0.37 | 0.65 | 0.577-0.74 | 0.00 | 1.40 | 1.21-1.62 | 0.00 | 0.00 |

a Reference group. b 0.1% missing; c 1.0% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **admissions ap status** | | | | | | | | | | | |
| **Outcomes measured year 6** | *AP 1 (Continuous AP)*a  *n=2140* | *AP 2 (Sustained discontinuation)*  *n=686* | | | *AP 3 (Non-sustained discontinuation)*  *n=11631* | | | *AP 4 (No AP)*  *n=6364* | | | *Total*  *N=20821* |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
| Employment (work or study) b |  | 2.65 | 1.94-3.61 | 0.00 | 2.33 | 1.89-2.88 | 0.00 | 6.88 | 5.58-8.49 | 0.00 | 0.00 |
| Living with partner c |  | 0.97 | 0.81-1.16 | 0.71 | 0.95 | 0.86-1.04 | 0.28 | 1.24 | 1.13-1.38 | 0.00 | 0.00 |
| Living with children c |  | 1.98 | 1.52-2.57 | 0.00 | 1.32 | 1.12-1.56 | 0.00 | 2.48 | 2.10-2.94 | 0.00 | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  |  |
| No alcohol misuse |  | 1.57 | 1.06-2.34 | 0.03 | 0.86 | 0.72-1.03 | 0.10 | 2.24 | 1.81-2.79 | 0.00 | 0.00 |
| No substance misuse |  | 0.87 | 0.63-1.21 | 0.42 | 0.59 | 0.49-0.70 | 0.00 | 1.33 | 1.09-1.63 | 0.01 | 0.00 |
| No involuntary admissions |  | 0.99 | 0.63-1.55 | 0.95 | 0.55 | 0.43-0.69 | 0.00 | 1.89 | 1.43-2.51 | 0.00 | 0.00 |
| No coercion |  | 1.21 | 0.86-1.70 | 0.28 | 0.62 | 0.52-0.73 | 0.00 | 2.53 | 2.05-3.12 | 0.00 | 0.00 |

a Reference group. b 0.1% missing; c 1.0% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **latest half ap status** | | | | | | | | | | | |
| **Outcomes measured year 6** | *AP 1 (Continuous AP)*a  *n=909* | *AP 2 (Sustained discontinuation)*  *n=401* | | | *AP 3 (Non-sustained discontinuation)*  *n=4979* | | | *AP 4 (No AP)*  *n=4255* | | | *Total*  *N=10544* |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | p value |
| Employment (work or study) b |  | 2.45 | 1.63-3.69 | 0.00 | 2.04 | 1.52-2.75 | 0.00 | 5.38 | 4.02-7.20 | 0.00 | 0.00 |
| Living with partner c |  | 1.02 | 0.80-1.30 | 0.90 | 1.05 | 0.90-1.21 | 0.54 | 1.31 | 1.13-1.52 | 0.00 | 0.00 |
| Living with children c |  | 1.66 | 1.18-2.33 | 0.00 | 1.18 | 0.94-1.49 | 0.15 | 1.88 | 1.50-2.36 | 0.00 | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  |  |
| No alcohol misuse |  | 1.06 | 0.66-1.70 | 0.82 | 1.02 | 0.77-1.34 | 0.92 | 1.66 | 1.23-2.23 | 0.00 | 0.00 |
| No substance misuse |  | 0.56 | 0.38-0.82 | 0.00 | 0.57 | 0.44-0.73 | 0.00 | 0.93 | 0.71-1.23 | 0.62 | 0.00 |
| No involuntary admissions |  | 0.50 | 0.29-0.87 | 0.02 | 0.52 | 0.35-0.78 | 0.00 | 1.09 | 0.72-1.65 | 0.70 | 0.00 |
| No coercion |  | 0.81 | 0.57-1.16 | 0.25 | 0.65 | 0.53-0.82 | 0.00 | 1.45 | 1.15-1.84 | 0.00 | 0.00 |

a Reference group. b < 0.0% missing; c 0.7% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| other F2 diagnosis preceding schizophrenia **ap status** | | | | | | | | | | | | |
| **Outcomes measured year 6** | *AP 1 (Continuous AP)*a  *n=1940* | *AP 2 (Sustained discontinuation)*  *n=703* | | | *AP 3 (Non-sustained discontinuation)*  *n=10124* | | | *AP 4 (No AP)*  *n=8054* | | | *Total*  *N=20821* | |
| Reference group | OR | 95% CI | p value | OR | 95% CI | p value | OR | 95% CI | p value | | p value |
| Employment (work or study) b |  | 2.54 | 1.87-3.46 | 0.00 | 2.02 | 1.62-2.50 | 0.00 | 5.41 | 4.37-6.70 | 0.00 | | 0.00 |
| Living with partner c |  | 1.00 | 0.83-1.19 | 0.98 | 0.96 | 0.86-1.06 | 0.37 | 1.11 | 1.00-1.23 | 0.06 | | 0.00 |
| Living with children c |  | 1.95 | 1.51-2.52 | 0.00 | 1.24 | 1.05-1.47 | 0.01 | 1.95 | 1.65-2.32 | 0.00 | | 0.00 |
| **Outcomes measured year 5-6** |  |  |  |  |  |  |  |  |  |  | |  |
| No alcohol misuse |  | 1.20 | 0.84-1.72 | 0.33 | 0.98 | 0.81-1.19 | 0.83 | 1.36 | 1.11-1.66 | 0.00 | | 0.00 |
| No substance misuse |  | 0.67 | 0.49-0.90 | 0.01 | 0.66 | 0.55-0.80 | 0.00 | 0.93 | 0.76-1.13 | 0.46 | | 0.00 |
| No involuntary admissions |  | 0.47 | 0.32-0.69 | 0.00 | 0.53 | 0.41-0.69 | 0.00 | 0.78 | 0.59-1.02 | 0.07 | | 0.00 |
| No coercion |  | 0.69 | 0.51-0.93 | 0.01 | 0.61 | 0.51-0.73 | 0.00 | 1.12 | 0.92-1.36 | 0.23 | | 0.00 |

a Reference group. b 0.1% missing; c 1.0% missing. Abbreviations: OR=Odds ratio, CI=Confidence interval

**Table S5. Sensitivity analyses of incidence rate and incidence rate ratio of psychiatric outpatient clinic contacts, hospital admissions, and length of stay with conservative ap status, half DDD ap status, admissions ap status, latest half ap status, and other F2 diagnosis preceding schizophrenia ap status.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Conservative ap status** | | | | | | | | | | | | | | | | | | |
| **Outcomes measured year**  **5-6**  **N=21348** | | *AP 1 (Continuous AP)*a  *n=4035* | | | | *AP 2 (Sustained discontinuation)*  *n=1365* | | | | *AP 3 (Non-sustained discontinuation)*  *n=7831* | | | | | *AP 4 (No AP)*  *n=8117* | | | |
| IR/IRR | 95% CI | p value model | | IR/IRR | 95% CI | p value | | IR/IRR | 95% CI | p value | | IR/ IRR | | | 95% CI | p value |
| Outpatient clinic contacts | IR | 9.72 | 9.12-10.36 | | 0.00 | 7.42 | 6.65-8.28 | |  | 11.35 | 10.84-11.88 | |  | 5.68 | | 5.43-5.95 | |  |
| IRR |  |  | |  | 0.76 | 0.67-0.87 | | 0.00 | 1.17 | 1.08-1.26 | | 0.00 | 0.59 | | 0.54-0.63 | | 0.00 |
| Number of admissions | IR | 0.40 | 0.36-0.44 | | 0.00 | 0.36 | 0.31-0.43 | |  | 0.51 | 0.47-0.54 | |  | 0.19 | | 0.18-0.21 | |  |
| IRR |  |  | |  | 0.92 | 0.76-1.10 | | 0.34 | 1.27 | 1.14-1.42 | | 0.00 | 0.49 | | 0.44-0.55 | | 0.00 |
| Length of admissions (days) | IR | 10.00 | 8.50-11.75 | | 0.00 | 11.91 | 9.02-15.73 | |  | 16.35 | 14.55-18.36 | |  | 8.10 | | 7.23-9.08 | |  |
| IRR |  |  | |  | 1.19 | 0.86-1.64 | | 0.29 | 1.64 | 1.34-2.00 | | 0.00 | 0.81 | | 0.67-0.99 | | 0.04 |

a Reference group. Abbreviations: IR=incidence rate, IRR= incidence rate ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **half DDD ap status** | | | | | | | | | | | | | | | |
| **Outcomes measured year**  **5-6**  **N=21348** | | *AP 1 (Continuous AP)*a  *n=5261* | | | *AP 2 (Sustained discontinuation)*  *n=1130* | | | *AP 3 (Non-sustained discontinuation)*  *n=8312* | | | | | *AP 4 (No AP)*  *n=6645* | | |
| IR/IRR | 95% CI | p value model | IR/IRR | 95% CI | p value | IR/IRR | | 95% CI | p value | IR/IRR | | 95% CI | p value |
| Outpatient clinic contacts | IR | 9.50 | 8.99-10.05 | 0.00 | 7.25 | 6.43-8.18 |  | 10.86 | 10.39-11.35 | |  | 5.41 | | 5.15-5.69 |  |
| IRR |  |  |  | 0.76 | 0.67-0.87 | 0.00 | 1.14 | 1.06-1.23 | | 0.00 | 0.57 | | 0.53-0.61 | 0.00 |
| Number of admissions | IR | 0.39 | 0.36-0.43 | 0.00 | 0.33 | 0.28-0.40 |  | 0.48 | 0.45-0.51 | |  | 0.19 | | 0.17-0.20 |  |
| IRR |  |  |  | 0.85 | 0.70-1.03 | 0.10 | 1.21 | 1.10-1.34 | | 0.00 | 0.47 | | 0.42-0.53 | 0.00 |
| Length of admissions (days) | IR | 9.53 | 8.27-10.99 | 0.00 | 13.62 | 10.03-18.50 |  | 15.69 | 14.02-17.57 | |  | 8.19 | | 7.22-9.29 |  |
| IRR |  |  |  | 1.43 | 1.02-2.00 | 0.04 | 1.65 | 1.37-1.97 | | 0.00 | 0.86 | | 0.71-1.04 | 0.12 |

a Reference group. Abbreviations: IR=incidence rate, IRR= incidence rate ratio, CI=Confidence interval

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **admissions ap status** | | | | | | | | | | | | | |
| **Outcomes measured year**  **5-6**  **N=21348** | | *AP 1 (Continuous AP)*a  *n=2192* | | | *AP 2 (Sustained discontinuation)*  *n=701* | | | *AP 3 (Non-sustained discontinuation)*  *n=11958* | | | *AP 4 (No AP)*  *n=6497* | | |
| IR/IRR | 95% CI | p value model | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value |
| Outpatient clinic contacts | IR | 10.80 | 9.94-11.74 | 0.00 | 7.84 | 6.76-9.09 |  | 11.27 | 10.87-11.68 |  | 3.15 | 3.00-3.32 |  |
| IRR |  |  |  | 0.73 | 0.61-0.86 | 0.00 | 1.04 | 0.95-1.14 | 0.37 | 0.29 | 0.27-0.32 | 0.00 |
| Number of admissions | IR | 0.40 | 0.36-0.45 | 0.00 | 0.21 | 0.17-0.27 |  | 0.51 | 0.49-0.54 |  | 0.08 | 0.07-0.08 |  |
| IRR |  |  |  | 0.53 | 0.41-0.69 | 0.00 | 1.28 | 1.13-1.46 | 0.00 | 0.19 | 0.16-0.22 | 0.00 |
| Length of admissions (days) | IR | 14.54 | 11.74-18.01 | 0.00 | 6.22 | 4.26-9.10 |  | 16.37 | 14.94-17.95 |  | 2.82 | 2.49-3.20 |  |
| IRR |  |  |  | 0.43 | 0.28-0.66 | 0.00 | 1.13 | 0.89-1.42 | 0.32 | 0.19 | 0.15-0.25 | 0.00 |

a Reference group. Abbreviations: IR=incidence rate, IRR= incidence rate ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **latest half ap status** | | | | | | | | | | | | | |
| **Outcomes measured year**  **5-6**  **N=10790** | | *AP 1 (Continuous AP)*a  *n=932* | | | *AP 2 (Sustained discontinuation)*  *n=414* | | | *AP 3 (Non-sustained discontinuation)*  *n=5110* | | | *AP 4 (No AP)*  *n=4334* | | |
| IR/IRR | 95% CI | p value model | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value |
| Outpatient clinic contacts | IR | 10.04 | 8.83-11.43 | 0.00 | 6.40 | 5.27-7.78 |  | 10.33 | 9.77-10.91 |  | 4.06 | 3.82-4.32 |  |
| IRR |  |  |  | 0.64 | 0.51-0.81 | 0.00 | 1.03 | 0.89-1.18 | 0.70 | 0.40 | 0.35-0.47 | 0.00 |
| Number of admissions | IR | 0.35 | 0.28-0.43 | 0.00 | 0.35 | 0.25-0.47 |  | 0.47 | 0.43-0.51 |  | 0.16 | 0.14-0.18 |  |
| IRR |  |  |  | 1.00 | 0.68-1.46 | 0.99 | 1.36 | 1.08-1.70 | 0.01 | 0.46 | 0.36-0.59 | 0.00 |
| Length of admissions (days) | IR | 7.75 | 5.40-11.14 | 0.00 | 7.97 | 4.63-13.72 |  | 12.54 | 10.74-14.64 |  | 4.46 | 3.77-5.28 |  |
| IRR |  |  |  | 1.03 | 0.54-1.97 | 0.94 | 1.62 | 1.09-2.40 | 0.02 | 0.58 | 0.39-0.86 | 0.01 |

a Reference group. Abbreviations: IR=incidence rate, IRR= incidence rate ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| other F2 diagnosis preceding schizophrenia **ap status** | | | | | | | | | | | | | |
| **Outcomes measured year**  **5-6**  **N=21348** | | *AP 1 (Continuous AP)* a  *n=1985* | | | *AP 2 (Sustained discontinuation)*  *n=721* | | | *AP 3 (Non-sustained discontinuation)*  *n=10392* | | | *AP 4 (No AP)*  *n=8250* | | |
| IR/IRR | 95% CI | p value model | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value | IR/IRR | 95% CI | p value |
| Outpatient clinic contacts | IR | 9.35 | 8.54-10.23 | 0.00 | 6.96 | 5.98-8.09 |  | 11.00 | 10.58-11.45 |  | 5.75 | 5.50-6.02 |  |
| IRR |  |  |  | 0.74 | 0.62-0.89 | 0.00 | 1.18 | 1.07-1.30 | 0.00 | 0.62 | 0.56-0.68 | 0.00 |
| Number of admissions | IR | 0.37 | 0.33-0.42 | 0.00 | 0.33 | 0.26-0.41 |  | 0.48 | 0.46-0.51 |  | 0.20 | 0.19-0.22 |  |
| IRR |  |  |  | 0.88 | 0.68-1.13 | 0.31 | 1.30 | 1.13-1.50 | 0.00 | 0.54 | 0.46-0.63 | 0.00 |
| Length of admissions (days) | IR | 8.71 | 6.92-10.97 | 0.00 | 12.83 | 8.75-18.81 |  | 15.06 | 13.61-16.66 |  | 8.28 | 7.39-9.28 |  |
| IRR |  |  |  | 1.47 | 0.94-2.30 | 0.09 | 1.73 | 1.34-2.22 | 0.00 | 0.95 | 0.74-1.23 | 0.70 |

a Reference group. Abbreviations: IR=incidence rate, IRR= incidence rate ratio, CI=Confidence interval

**Table S6. Sensitivity analyses of hazard ratios of death by all causes and death by suicide during year 5-6 with conservative ap status, half DDD ap status, admissions ap status, latest half ap status, and other F2 diagnosis preceding schizophrenia ap status.**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Conservative ap status** | | | | | | | | | | | |
| **Outcomes measured year 5-6** | *AP 1 (Continuous AP)*a | *AP 2 (Sustained discontinuation)* | | | *AP 3 (Non-sustained discontinuation)* | | | *AP 4 (No AP)* | | | *Total* |
| Reference group | HR | 95% CI | p value | HR | 95% CI | p value | HR | 95% CI | p value | p value model |
| Death by all causes |  | 0.63 | 0.36-1.11 | 0.11 | 0.68 | 0.50-0.93 | 0.01 | 0.76 | 0.56-1.03 | 0.07 | 0.09 |
| Death by suicide |  | 2.01 | 0.34-12.00 | 0.45 | 3.00 | 0.88-10.25 | 0.08 | 0.82 | 0.20-3.45 | 0.79 | 0.03 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **half DDD ap status** | | | | | | | | | | | |
| **Outcomes measured year 5-6** | *AP 1 (Continuous AP)*a | *AP 2 (Sustained discontinuation)* | | | *AP 3 (Non-sustained discontinuation)* | | | *AP 4 (No AP)* | | | *Total* |
| Reference group | HR | 95% CI | p value | HR | 95% CI | p value | HR | 95% CI | p value | p value model |
| Death by all causes |  | 0.63 | 0.34-1.15 | 0.13 | 0.79 | 0.60-1.05 | 0.10 | 0.64 | 0.47-0.87 | 0.01 | 0.03 |
| Death by suicide |  | 3.56 | 0.80-15.90 | 0.10 | 2.77 | 0.13-2.65 | 0.07 | 0.59 | 0.13-2.65 | 0.50 | 0.01 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **admissions ap status** | | | | | | | | | | | |
| **Outcomes measured year 5-6** | *AP 1 (Continuous AP)* a | *AP 2 (Sustained discontinuation)* | | | *AP 3 (Non-sustained discontinuation)* | | | *AP 4 (No AP)* | | | *Total* |
| Reference group | HR | 95% CI | p value | HR | 95% CI | p value | HR | 95% CI | p value | p value model |
| Death by all causes |  | 0.69 | 0.32-1.49 | 0.35 | 0.84 | 0.58-1.20 | 0.33 | 0.71 | 0.48-1.06 | 0.09 | 0.36 |
| Death by suicide |  | 1.59 | 0.14-17.50 | 0.71 | 1.99 | 0.47-8.50 | 0.35 | 0.51 | 0.09-3.05 | 0.46 | 0.07 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **latest half ap status** | | | | | | | | | | | | |
| **Outcomes measured year 5-6** | *AP 1 (Continuous AP)* a | *AP 2 (Sustained discontinuation)* | | | *AP 3 (Non-sustained discontinuation)* | | | | *AP 4 (No AP)* | | | *Total* |
| Reference group | HR | 95% CI | p value | HR | 95% CI | p value | | HR | 95% CI | p value | p value model |
| Death by all causes |  | 0.67 | 0.25-1.80 | 0.42 | 0.57 | 0.33-0.98 | | 0.04 | 0.53 | 0.30-0.93 | 0.03 | 0.20 |
| Death by suicide |  | 1.17 | 0.11-12.87 | 0.90 | 0.66 | 0.14-3.17 | | 0.60 | 0.33 | 0.05-1.95 | 0.22 | 0.53 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| other F2 diagnosis preceding schizophrenia **ap status** | | | | | | | | | | | |
| **Outcomes measured year 5-6** | *AP 1 (Continuous AP* a | *AP 2 (Sustained discontinuation)* | | | *AP 3 (Non-sustained discontinuation)* | | | *AP 4 (No AP)* | | | *Total* |
| Reference group | HR | 95% CI | p value | HR | 95% CI | p value | HR | 95% CI | p value | p value model |
| Death by all causes |  | 0.58 | 0.26-1.32 | 0.19 | 0.77 | 0.53-1.12 | 0.18 | 0.81 | 0.55-1.19 | 0.28 | 0.07 |
| Death by suicide |  | 1.45 | 0.13-16.00 | 0.76 | 1.92 | 0.45-8.26 | 0.38 | 0.65 | 0.13-3.35 | 0.60 | 0.13 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval

**Table S7. Hazard ratios of death by all causes and death by suicide during year 2-5 with AP exposure as a time-varying covariate**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcomes measured year 2-5** | AP 1 (Continuous AP) | AP 2 (Sustained discontinuation) | | | AP 3 (Non-sustained discontinuation) | | | AP 4 (No AP) | | | Total |
| Reference group a | HR | 95% CI | p value | HR | 95% CI | p value | HR | 95% CI | p value | p value model |
| Death by all causes |  | 1.19 | 0.82-1.71 | 0.36 | 1.07 | 0.87-1.33 | 0.51 | 1.35 | 1.02-1.52 | 0.03 | 0.07 |
| Death by suicide |  | 5.49 | 1.83-16.47 | 0.00 | 4.43 | 1.83-10.72 | 0.00 | 2.25 | 0.95-5.33 | 0.07 | 0.00 |

a Reference group. Abbreviations: HR=Hazard ratio, CI=Confidence interval