**Other Supplementary Material**

In addition to analysing data regarding transition from SIPD to schizophrenia, we also analysed the transition from SIPD to a broader diagnostic category of schizophrenia-spectrum disorders. This allowed comparison to be made with other published studies (Arendt *et al* 2005; Niemi-Pynttari *et al* 2013), which also used this broader definition.

**Methods**

Schizophrenia spectrum disorders were considered to be diagnoses coded F22 and F23, persistent delusional disorder and acute and transient psychotic disorders, respectively, plus schizophrenia (F20). Methods were otherwise as above.

**Results**

**Whole sample characteristics**

Table One summarises results for those with the diagnosis of schizophrenia spectrum disorders (F20, F22 and 23), of whom 720 patients were identified (20.7%). Compared to those who were not later admitted to hospital with this diagnosis, the male to female ratio of 4.5:1 remained significantly higher (χ2(1, *N* = 3486) =19.17, *p*<0.001), there was a statistically significant younger age of first presentation of 29.5 years (SD=10.7) vs 34.8 years (SD=13.3); *t*(1357)=11.37, *p*<0.001 and mean length of stay in hospital was longer but again not statistically significant: 34.4 days (SD=160.6) vs. 30.3 days (SD=491.7); *t*(3339)=-0.37, *p*=0.715.

**Whole sample transition rate and mean time to change to schizophrenia spectrum disorders**

Kaplan-Meier survival analysis with censoring over the full 15.5-year period revealed the mean survival time of the entire dataset from first recorded diagnosis of SIPD to specific diagnosis of schizophrenia spectrum disorder to be 12.5 years (95%CI: 12.3-12.7). The cumulative hazard rate was 24.3% (SE=0.008). Examination of covariates found that male gender, length of first admission (more than 14 days) and age at first admission (less than 30 years) were significant risk factors with hazard ratios of 1.4 (95%CI: 1.2-1.7), *p*=0.001, for male sex, 1.7 (95%CI 1.5-2.0), *p*<0.001, for longer first admission, and 2.3 (95%CI: 2.0-2.8), *p*<0.001 for younger age at first admission. Although none of the specific substances were significantly more likely than any other to be associated with the development of a schizophrenia spectrum disorder, alcohol and opiates were significantly less likely to be associated, with hazard ratios of 0.69 (95%CI: 0.56-0.85), *p*<0.001, and 0.73 (95%CI 0.57-0.94), *p*=0.013, respectively. Table Two shows hazard ratios for development of schizophrenia spectrum disorders for those with SIPD induced by opioids, cannabis, stimulants and multiple/other drugs, compared with alcohol, the group for which the risk was lowest. The risk of developing a schizophrenia spectrum disorder was significantly greater for all of the other groups when compared to the alcohol-induced psychotic disorder group, where the risk was lowest. Between group comparisons for the risk of opioid, cannabis, stimulant and multiple/other drug-induced episodes of psychosis leading to schizophrenia spectrum disorder showed no significant differences.

For those later diagnosed with a schizophrenia spectrum disorder, mean time to change in diagnosis was 2.3 years (SD 2.6) and median time to change in diagnosis was 1.4 years (range 0-13.5 years). 43.9% had converted within one year of first presentation SIP and the conversion rates at two, three, four and five years were 59.9%, 71.7%, 80%, and 85.3% respectively.

**Discussion**

The rate of transition to schizophrenia spectrum disorder following an episode of SIPD was estimated at 24.3%, compared with a lower rate of 17.3% for the narrower diagnosis of schizophrenia. This held true for analysis of transition broken down by specific substance, with rates for transition being higher for schizophrenia spectrum disorder than schizophrenia. However, all rates estimated in the present study were lower than those found in other studies (Arendt *et al* 2005; Niemi-Pynttari *et al* 2013). The reasons for this difference are unclear, but may relate to differences in patterns of substance use, or differences in diagnostic practice. Considering the risk of transition to a more broadly defined schizophrenia spectrum disorder, rather than using the narrower category of schizophrenia, emphasises the importance of long-term follow up for patients diagnosed with an acute SIPD.

**Table 1**

**Summary of patient demographics and risk to conversion to diagnosis of schizophrenia spectrum disorder across specific substance induced psychotic disorder sub-groups**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **ICD-10 Code** | **Substance** | **Total****n** | **Men****n (%)** | **Women** **n (%)** | **Age mean (sd) yrs** | **Cumulative hazard (with censoring)****Schizophrenia****Spectrum****(F20,22,23)****% (SE)** |
| F10.5 | Alcohol | 1038 | 801(83.5) | 237(16.5) | 44.5(13.1) | 15.7 (1.2) |
| F11.5 | Opioids | 419 | 309(73.7) | 110(26.3) | 30.1(10.1) | 23.4 (2.6) |
| F12.5 | Cannabis | 276 | 214(77.5) | 62(22.5) | 28.2(9.1) | 30.4 (3.2) |
| F13.5 | Sedatives | 35 | 20 (57.1) | 15(42.9) | 33.8(13.3) | 20.6 (7.8) |
| F14.5 | Cocaine | 24 | 20(83.3) | 4(16.7) | 28.9(7.4) | 27.8 (9.9) |
| F15.5 | Stimulants | 273 | 183(67.0) | 90(33.0) | 30.4(10.6) | 27.2 (3.1) |
| F16.5 | Hallucinogens | 36 | 26(72.2) | 10(27.8) | 23.2(6.5) | 18.2 (6.8) |
| F17.5 | Tobacco | 2 | 1(50) | 1(50) | 46.5(20.5) | 50.0 (35.4) |
| F18.5 | Solvents | 14 | 12(85.7) | 2(14.3) | 27.1(9.5) | 22.1 (14.1) |
| F19.5 | Multiple / Other | 1369 | 1048(76.6) | 321(23.4) | 28.8(9.4) | 30.0 (1.5) |
| All | Any | 3486 | 2634(75.6) | 852(24.4) | 33.9(12.9) | 24·3(0.008) |

**Table 2**

**Risk for Conversion of Substance-Induced Psychotic Disorder to Schizophrenia Spectrum Disorder**

|  |  |
| --- | --- |
| **Substance Inducing Psychosis** | **Hazard ratio for conversion to schizophrenia spectrum disorder****\*(95% CI); P value** |
| F10.5 Alcohol | 1 |
| F11.5 Opioids | 1.439 (1.094 – 1.894); p=0.00933 |
| F12.5 Cannabis | 2.215 (1.669 – 2.940); p<0.0001 |
| F15.5 Stimulants | 1.884 (1.406 – 2.525); p<0.0001 |
| F19.5 Multiple / Other | 2.055 (1.691 – 2.498); p<0.0001 |

**\*** Hazard ratio of 1 indicates the comparator group

**References**

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