**Supplementary material, Methods**

**Background variables and covariates**

*Age of illness onset*, defined as the age when the first evident psychotic symptoms emerged, was ascertained from medical records.

*Level of education* was based on questionnaire information gained in the 43-year study on the level of basic education (O level, 9 years or A level, 12 years) and vocational education (none, course or school, currently studying, college, polytechnic or university) which were combined and classified into three categories: low = O level with low vocational education (none, course or school or currently studying), middle = O level with high vocational education (college, polytechnic or university) or A level with low vocational education and high = A level with high vocational education.

*Occupational status* at the time of the 43-year study was classified into three categories: 1) working, if the subjects were studying, on maternity leave or in full-time or part-time work, 2) on disability pension, if they were retired because of psychiatric or other illness or 3) not working, if they were unemployed, or outside of working life for other reasons. Information was ascertained in an interview in the 43-years study and missing information was completed with Finnish Centre for Pension registers data.

*Alcohol abuse diagnosis* included subjects with an earlier or current diagnosis of either alcohol abuse or dependency evaluated in the SCID I interview at the 43-year study.

*PANSS* (Positive and Negative Syndrome Scale) [1] *scores* were evaluated in a PANSS specific interview at the 43-years study. PANSS total symptoms were measured from one week before the interview and divided into positive, negative and disorganisation symptoms based on the model described by van der Gaag et al. [2]. PANSS was also utilised in determining remission status (more below).

*The Severity of Illness subscale of the CGI* (Clinical Global Impression) [3], ranging from 1 (not ill at all) to 7 (among the most extremely ill), was ascertained in the interview at the 43-year study.

*Cumulative number of hospital treatment days* was obtained from the Care Register for Health Care (formerly Finnish Hospital Discharge Register).

*Psychiatric treatment status* was ascertained in the interview at the 43-year study by asking about previous and current psychiatric treatment contacts (place and time of starting the contact, frequency of visits) and grouped to four categories: no treatment contact, non-regular outpatient treatment (less frequent than once per month or of unknown frequency), regular outpatient treatment (visits in the psychiatric services or outpatient rehabilitation group at least once and mostly 1-4 times per month), and inpatient/institution (psychiatric hospital treatment or living in a sheltered home).

*Remission,* according to the Andreasen symptomatic criteria [4], was defined as having no symptoms (PANSS) at the time of the 43-year study and no psychiatric hospital treatments in 6 months before the study.

**Supplementary Table 1. Lifetime use and current use of psychiatric medications at 43 years of age in**

**schizophrenia (n=60).**

|  |  |  |  |
| --- | --- | --- | --- |
| **ATC code** | **Generic name** | **Lifetime use** | **Current use** |
| **n (%)** | **DDD years,** **mean (Sd)** | **n (%)** | **DDD,** **mean (Sd)** |
| **Antipsychotic medication** | 59 (98%) | 18.2 (20.2) | 51 (85%) | 1.6 (1.3) |
| **Typical antipsychotics** | 54 (90%) | 9.9 (14.0) | 19 (32%) | 0.7 (0.8) |
| N05AA01 | Chlorpromazine | 22 (37%) | 2.4 (5.8) | - | - |
| N05AA02 | Levomepromazine | 26 (43%) | 0.9 (2.1) | 4 (7%) | 0.4 (0.3) |
| N05AA03 | Promazine | 20 (33%) | 0.5 (0.9) | 1 (2%) | 0.7 |
| N05AB01 | Dixyrazine | 1 (2%) | 0.01 | - | - |
| N05AB02 | Fluphenazine | 2 (3%) | 20.1 (28.5) | - | - |
| N05AB03 | Perphenazine | 36 (60%) | 1.4 (2.1) | 6 (10%) | 0.6 (0.4) |
| N05AB08 | Thioproperazine | 1 (2%) | 4.3 | - | - |
| N05AC01 | Periciazine | 1 (2%) | 0.04 | - | - |
| N05AC02 | Thioridazine | 38 (63%) | 4.2 (6.3) | 1 (2%) | 0.7 |
| N05AC04 | Pipotiazine | 3 (5%) | 2.6 (3.8) | - | - |
| N05AD01 | Haloperidol | 40 (67%) | 2.4 (3.9) | 2 (3%) | 0.5 (0.07) |
| N05AD03 | Melperone | 3 (5%) | 0.03 (0.04) | - | - |
| N05AF01 | Flupentixol | 4 (7%) | 0.4 (0.4) | - | - |
| N05AF03 | Chlorprothixene | 15 (25%) | 1.1 (1.7) | 4 (7%) | 0.5 (0.2) |
| N05AF05 | Zuclopenthixol | 21 (35%) | 3.2 (5.6) | 3 (5%) | 1.5 (0.9) |
| N05AG02 | Pimozide | 1 (2%) | 0.4 | - | - |
| N05AL01 | Sulpiride | 7 (12%) | 0.1 (0.1) | - | - |
| N05AL04 | Remoxipride | 2 (3%) | 0.1 (0.006) | - | - |
| **Atypical antipsychotics** | 49 (82%) | 11.0 (9.9) | 43 (72%) | 1.6 (0.9) |
| N05AE03 | Sertindole | 3 (5%) | 0.4 (0.4) | - | - |
| N05AE04 | Ziprasidone | 1 (2%) | 0.06 | - | - |
| N05AH02 | Clozapine | 16 (27%) | 12.1 (13.3) | 11 (18%) | 1.4 (0.4) |
| N05AH03 | Olanzapine | 31 (52%) | 6.7 (7.6) | 20 (33%) | 1.7 (0.9) |
| N05AH04 | Quetiapine | 19 (32%) | 2.3 (3.9) | 7 (12%) | 1.1 (0.9) |
| N05AH05 | Asenapine | 1 (2%) | 0.03 | - | - |
| N05AX08 | Risperidone | 36 (60%) | 2.2 (3.7) | 4 (7%) | 0.9 (0.5) |
| N05AX12 | Aripiprazole | 11 (18%) | 1.1 (1.2) | 7 (12%) | 0.9 (0.8) |
| **Benzodiazepines** | 43 (72%) | 8.9 (10.2) | 23 (38%) | 1.2 (1.1) |
| N03AE01 | Clonazepam | 9 (15%) | 2.3 (3.2) | 3 (5%) | 0.6 (0.8) |
| N05BA01   | Diazepam  | 37 (62%) | 3.7 (5.2) | 8 (13%) | 0.9 (0.9) |
| N05BA02   | Chlordiazepoxide  | 9 (15%) | 2.2 (5.2) | 1 (2%) | 0.8 |
| N05BA04   | Oxazepam  | 27 (45%) | 1.7 (3.4) | 5 (8%) | 0.4 (0.3) |
| N05BA05   | Potassium clorazepate  | 9 (15%) | 1.1 (1.6) | - | - |
| N05BA06   | Lorazepam  | 13 (22%) | 0.8 (0.6) | 4 (7%) | 1.3 (0.8) |
| N05BA12   | Alprazolam  | 4 (7%) | 0.3 (0.2) | - | - |
| N05CD02   | Nitrazepam  | 7 (12%) | 0.6 (0.9) | - | - |
| N05CD05   | Triazolam  | 3 (5%) | 0.6 (0.7) | - | - |
| N05CD07   | Temazepam  | 34 (57%) | 2.4 (3.6) | 7 (12%) | 0.9 (0.5) |
| N05CD08   | Midazolam  | 4 (7%) | 0.009 (0.009) | - | - |
| N05CF01   | Zopiclone  | 25 (42%) | 1.8 (3.2) | 5 (8%) | 0.7 (0.3) |
| N05CF02   | Zolpidem  | 5 (8%) | 1.0 (0.9) | - | - |
| **Antidepressants** | 25 (42%) | 6.9 (6.7) | 13 (22%) | 1.3 (0.5) |
| N06AA04 | Clomipramine  | 1 (2%) | 0.008 | - | - |
| N06AA09 | Amitriptyline  | 10 (17%) | 2.2 (3.1) | 3 (5%) | 0.9 (0.7) |
| N06AA10 | Nortriptyline  | 1 (2%) | 0.007 | 1 (2%) | 0.07 |
| N06AA12 | Doxepin  | 3 (5%) | 0.1 (0.2) | 1 (2%) | 0.06 |
| N06AA21 | Maprotiline  | 1 (2%) | 0.6 | - | - |
| N06AB03 | Fluoxetine  | 9 (15%) | 3.5 (4.7) | 3 (5%) | 1.3 (0.6) |
| N06AB04 | Citalopram  | 13 (22%) | 4.1 (5.8) | 2 (3%) | 1.1 (0.2) |
| N06AB05 | Paroxetine  | 4 (7%) | 7.0 (4.6) | 1 (2%) | 2.0 |
| N06AB06 | Sertraline  | 5 (8%) | 3.4 (3.2) | 1 (2%) | 2.0 |
| N06AB08 | Fluvoxamine  | 1 (2%) | 0.5 | - | - |
| N06AB10 | Escitalopram  | 1 (2%) | 1.0 | 1 (2%) | 1.0 |
| N06AG02 | Moclobemide  | 1 (2%) | 0.004 | - | - |
| N06AX03 | Mianserin  | 2 (3%) | 1.4 (1.9) | - | - |
| N06AX11 | Mirtazapine  | 4 (7%) | 3.2 (3.9) | 2 (3%) | 1.0 (0.7) |
| N06AX16 | Venlafaxine  | 1 (2%) | 2.0 | 1 (2%) | 0.8 |
| N06AX17 | Milnacipran  | 1 (2%) | 0.09 | - | - |
| **Anticholinergic agents** |  |  |  |  |
| N04AA02   | Biperiden | 26 (43%) | 1.4 (2.7) | - | - |
| **Other medications** |  |  |  |  |
| G02CB01 | Bromocriptine | 1 (2%) | 0.01 | - | - |
| N03AB02   | Phenytoin  | 2 (3%) | 6.9 (8.5) | - | - |
| N03AF01   | Carbamazepine  | 5 (8%) | 2.9 (4.3) | 1 (2%) | 0.07 |
| N03AF02   | Oxcarbazepine  | 1 (2%) | 0.06 | - | - |
| N03AG01   | Valproic acid  | 10 (17%) | 6.3 (5.8) | 10 (17%) | 0.8 (0.4) |
| N03AX09   | Lamotrigine  | 3 (5%) | 0.5 (0.9) | 1 (2%) | 0.7 |
| N03AX11   | Topiramate  | 1 (2%) | 1.4 | - | - |
| N03AX14   | Levetiracetam  | 1 (2%) | 0.01 | - | - |
| N03AX16   | Pregabalin  | 1 (2%) | 0.03 | - | - |
| N04BC05 | Pramipexole | 1 (2%) | 0.02 | - | - |
| N05BB01   | Hydroxyzine  | 8 (13%) | 0.3 (0.4) | 1 (2%) | 1.3 |
| N05CC01 | Chloral hydrate | 1 (2%) | 0.002 | - | - |
| N05CH01 | Melatonin  | 2 (3%) | 0.9 (1.2) | 2 (3%) | 1.5 (0.7) |
| R06AD02 | Promethazine | 1 (2%) | 0.003 | - | - |

Means and standard deviations (Sd) are calculated for those who have used the specific medication.

**References**

[1] Kay SR, Opler LA, Fiszbein A. Positive and Negative Syndrome Scale (PANSS). In: Rush AJ, editor. American Psychiatric Association. Handbook of Psychiatric Measures, Washington: American Psychiatric Association; 2000, p. 734–736.

[2] van der Gaag M, Hoffman T, Remijsen M, Hijman R, de Haan L, van Meijel B, et al. The five factor model of the positive and negative syndrome scale II: a ten-fold cross-validation of a revised model. Schizophr Res 2006;85:280–7.

[3] Guy W. Clinical Global Impressions (CGI) Scale. In: American Psychiatric Association. Handbook of Psychiatric Measures, Washington: American Psychiatric Association; 2000.

[4] Andreasen NC, Carpenter WT, Kane JM, Lasser RA, Marder SR, Weinberger DR. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry 2005;162:441–9.