Treatment of Major Depressive Disorder in Japanese Patients With Cancer: A Matched Cohort Study Using Employer-based Health Insurance Claims Data

Tatsuo AKECHI*
Shinji FUJIMOTO
Izumi MISHIRO
Katsuhito MURASE

*Author for correspondence:
Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan
Email: takechi@med.nagoya-cu.ac.jp

Table S1  ATC codes used to classify drugs prescribed for depression

| Drug class                                      | ATC code | ATC code name          | Generic name                                                                 |
|------------------------------------------------|----------|------------------------|------------------------------------------------------------------------------|
| **Antidepressants**                            |          |                        |                                                                              |
| SSRI                                           | N06A4    | SSRI antidepressants   | Fluvoxamine maleate                                                          |
|                                                |          |                        | Paroxetine hydrochloride hydrate                                             |
|                                                |          |                        | Sertraline hydrochloride                                                     |
|                                                |          |                        | Escitalopram oxalate                                                        |
| SNRI                                           | N06A5    | SNRI antidepressants   | Milnacipran hydrochloride                                                     |
|                                                |          |                        | Duloxetine hydrochloride                                                     |
|                                                |          |                        | Venlafaxine hydrochloride                                                    |
| NaSSA                                          | N06A9    | Antidepressants, all others | Mirtazapine                                                                |
| Conventional antidepressants, including tricyclic antidepressants | N06A9 | Antidepressants, all others | Amitriptyline hydrochloride                                                   |
|                                                |          |                        | Amoxapine                                                                    |
|                                                |          |                        | Imipramine hydrochloride                                                     |
|                                                |          |                        | Clomipramine hydrochloride                                                   |
|                                                |          |                        | Setiptiline maleate                                                          |
|                                                |          |                        | Trazodone hydrochloride                                                      |
|                                                |          |                        | Nortriptyline hydrochloride                                                  |
|                                                |          |                        | Maprotiline hydrochloride                                                    |
|                                                |          |                        | Mianserin hydrochloride                                                      |
|                                                |          |                        | Lofepramine hydrochloride                                                    |
|                                                |          |                        | Dosulepin hydrochloride                                                      |
|                                                |          |                        | Trimipramine maleate                                                         |
| Sulpiride                                      | N05A9    | Conventional antipsychotics | Sulpiride,                                                                     |
| Alprazolam                                     | N05C     | Anxiolytics (minor tranquilizers) | Alprazolam |
| Other drugs          | N05B1 | Non-barbiturates, plain | Estazolam          |
|---------------------|-------|-------------------------|--------------------|
|                     |       |                         | Quazepam           |
|                     |       |                         | Triazolam          |
|                     |       |                         | Nitrazepam         |
|                     |       |                         | Nimetazepam        |
|                     |       |                         | Haloxazolam        |
|                     |       |                         | Flunitrazepam      |
|                     |       |                         | Flurazepam         |
|                     |       |                         | Flurazepam hydrochloride |
|                     |       |                         | Brotizolam         |
|                     |       |                         | Rilmazafone hydrochloride hydrate |
|                     |       |                         | Lormetazepam       |
| N05C                | Anxiolytics (minor tranquilizers) | Etizolam |
|                     |       |                         | Oxazolam           |
|                     |       |                         | Cloxazolam         |
|                     |       |                         | Clotiazepam        |
|                     |       |                         | Clorazepate dipotassium |
|                     |       |                         | Chlordiazepoxide   |
|                     |       |                         | Diazepam           |
|                     |       |                         | Tofisopam          |
|                     |       |                         | Fludiazepam        |
|                     |       |                         | Flutazolam         |
|                     |       |                         | Flutoprazepam      |
|                     |       |                         | Bromazepam         |
|                     |       |                         | Prazeplam          |
|                     |       |                         | Mexazolam          |
|                     |       |                         | Medazepam          |
|                     |       |                         | Ethyl loflazepate  |
|                     |       |                         | Lorazepam          |
| Non-BZD             | N05B1 | Non-barbiturates, plain | Eszopiclon         |
|                     |       |                         | Zopiclon           |
|                     |       |                         | Zolpidem tartrate  |
| Other sleeping      | N05B1 | Non-barbiturates, plain | Suvorexant         |
| drugs               |       |                         | Ramelteon          |
| Other non-barbiturates, plain | N05B1 | Non-barbiturates, plain | Triclofos sodium   |
|                     |       |                         | Bromovalerylurea   |
|                     |       |                         | Chlortal hydrate   |
|                     |       |                         | Potassium bromide  |
| Other anxiolytics | N05C | Anxiolytics (minor tranquilizers) | Calcium bromide  
| Sodium bromide |
| Atypical antipsychotics | N05A1 | Atypical antipsychotics | Tandospirone citrate  
| Hydroxyzine pamoate  
| Hydroxyzine hydrochloride  
| Anxiolytics (minor tranquilizers) |  
| Tandospirone citrate |  
| Hydroxyzine pamoate |  
| Hydroxyzine hydrochloride |  
| Other anxiolytics | N05C | Anxiolytics (minor tranquilizers) | Calcium bromide  
| Sodium bromide |
| Atypical antipsychotics | N05A1 | Atypical antipsychotics | Tandospirone citrate  
| Hydroxyzine pamoate  
| Hydroxyzine hydrochloride|
| Atypical antipsychotics | N05A1 | Atypical antipsychotics | Asenapine maleate  
| Aripiprazole |  
| Olanzapine |  
| Quetiapine fumarate |  
| Clozapine |  
| Zotepine |  
| Paliperidone |  
| Paliperidone palmitate |  
| Brexpiprazole |  
| Bionanserin |  
| Perospirone hydrochloride  
| hydrate |  
| Risperidone |  
| Conventional antipsychotics | N05A9 | Conventional antipsychotics | Oxpertine  
| Caripipramine maleate |  
| Caripipramine hydrochloride  
| hydrate |  
| Clozapine |  
| Chlorpromazine phenolphthalinate |  
| Chlorpromazine hydrochloride |  
| Chlorpromazine hydrochloride, promethazine  
| hydrochloride, phenobarbital |  
| Spiperone |  
| Sultopride hydrochloride |  
| Tiapride hydrochloride |  
| Thioridazine |  
| Thioridazine hydrochloride |  
| Timiperone |  
| Trifluoperazine maleate |  
| Nemonapride |  
| Haloperidol |  
| Haloperidol decanoate |  
| Pipamperone hydrochloride |  
| Pimozide |
| Fluphenazine enanthate | Fluphenazine decanoate | Fluphenazine maleate |
|------------------------|-----------------------|---------------------|
| Bromperidol            | Prochlorperazine maleate | Prochlorperazine mesilate |
| Propericiazine         | Perphenazine           | Perphenazine fendizoate |
| Perphenazine maleate   | Mosapramine hydrochloride | Moperone Hydrochloride |
| Levomepromazine maleate | Levomepromazine hydrochloride | Perphenazine hydrochloride |

| Barbiturates, plain | N05B3 | Barbiturates, plain |
|---------------------|-------|---------------------|
| Amobarbital         |       | Amobarbital sodium  |
| Secobarbital sodium |       | Barbital            |
| Phenobarbital       |       | Phenobarbital sodium|
| Pentobarbital calcium |     | Pentobarbital sodium|

| Herbal hypnotics/ sedatives | N05B5 | Herbal hypnotics/sedatives |
|-----------------------------|-------|----------------------------|
| Passiflora extract          |       |                            |

| Mood stabilizers (antimania drug) | N06A3 | Mood stabilizers (antimania drug) |
|-----------------------------------|-------|-----------------------------------|
| Lithium carbonate                 |       |                                   |

**ATC Anatomical Therapeutic Chemical system, BZD benzodiazepine, NaSSA noradrenergic and specific serotonergic antidepressant, SNRI serotonin noradrenaline reuptake inhibitor, SSRI selective serotonin reuptake inhibitors**
| Drug class/name, n (%) (95% CI) | Sex | Age | <40 years | 40–64 years | ≥65 years | <100 beds | ≥100 beds |
|---|---|---|---|---|---|---|---|
| No treatment | n=283 | n=357 | n=71 | n=486 | n=83 | NA | NA |
| Antidepressants | n=1199 | n=1186 | n=363 | n=1836 | n=186 | n=185 | n=530 |
| SSRI | n=527 | n=597 | n=188 | n=867 | n=69 | n=912 | n=210 |
| SNRI | n=298 | n=390 | n=37 | n=372 | n=118 | n=118 | n=118 |
| NaSSA | n=138 | n=101 | n=38 | n=179 | n=22 | n=161 | n=78 |
| Conventional | n=218 | n=228 | n=56 | n=332 | n=58 | n=321 | n=123 |
| Sulpiride | n=24 | n=16 | n=4 | n=33 | n=3 | n=37 | n=3 |
| Alprazolam | n=142 | n=185 | n=65 | n=261 | n=11 | n=268 | n=59 |
| Other medications | n=1129 | n=1242 | n=352 | n=1835 | n=184 | n=1284 | n=330 |
| BZD | n=917 | n=1014 | n=1505 | n=146 | n=116 | n=56 | n=1056 |
| Non-BZD | n=248 | n=213 | n=68 | n=358 | n=35 | n=272 | n=73 |
| Other sleep medication | n=59 | n=65 | n=19 | n=59 | n=6 | n=67 | n=28 |
| Other non-barbiturate (single agent) | n=3 | n=6 | n=0 | n=0 | n=0 | n=0 | n=0 |
| Other anxiolytic | n=19 | n=31 | n=10 | n=34 | n=6 | n=22 | n=6 |
| Atypical antipsychotic | n=62 | n=116 | n=34 | n=132 | n=12 | n=89 | n=40 |
| Barbiturate (single agent) | n=2 | n=1 | n=0 | n=5 | n=0 | n=3 | n=1 |
| Typical antipsychotic | n=21 | n=17 | n=3 | n=31 | n=4 | n=16 | n=7 |
| Herbal | n=6 | n=0 | n=0 | n=0 | n=4 | n=0 | n=0 |
| Hypnotics/sedatives | n=12 | n=16 | n=6 | n=22 | n=0 | n=13 | n=8 |
| Mood stabilizers | n=6 | n=7 | n=10 | n=0 | n=0 | n=0 | n=0 |

BZD benzodiazepine, CI confidence interval. NA not applicable, NaSSA noradrenergic and specific serotonin antidepressant, SNRI serotonin noradrenaline reuptake inhibitor, SSRI selective serotonin reuptake inhibitor.
aExcludes four patients with no information about hospital size
bIndicates significant difference between men and women based on non-overlapping 95% CIs
cIndicates significant difference between age subgroups 40–64 years and ≥65 years based on non-overlapping 95% CIs
dIndicates significant difference between <100 beds and ≥100 beds based on non-overlapping 95% CIs