Supplementary Information

Article title: An Exploratory Study of Factors Associated with Long-Term, High-Dose Opioid Prescription in Cancer Patients in Japan Based on a Medical Claims Database

Journal name: Supportive Care in Cancer

Author names: Tatsuya Hashimoto, Hirokazu Mishima, Chika Sakai, Yuichi Koretaka, Yoji Saito

Correspondence to:
Tatsuya Hashimoto
Affiliation: Department of Anesthesiology, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane, Japan
Email: hashit@med.shimane-u.ac.jp
Supplement 1. ICD-10 codes for cancers included in the analysis

| ICD 10 code | Terms                                      |
|-------------|--------------------------------------------|
| C00-C14     | lip, oral cavity, and pharynx              |
| C15-C26     | esophagus                                  |
| C30-C39     | stomach                                    |
| C40-C41     | small intestine                            |
| C43-C44     | large intestine, anus, and anal            |
| C45-C49     | liver and intrahepatic bile ducts          |
| C50         | gallbladder and unspecified parts of biliary tract |
| C51-C58     | pancreas                                   |
| C60-C63     | other and ill-defined digestive organs     |
| C64-C68     | respiratory and intrathoracic organs       |
| C69-C72     | bone and articular cartilage               |
| C73-C75     | melanoma and other malignant neoplasms of skin |
| C76-C80     | mesothelial and soft tissue                |
| C81-C96     | breast                                     |
| C97         | female genital organs                      |
| D00         | male genital organs                        |
| D01         | urinary tract                              |
| D02         | eye, brain, and other parts of central nervous system |
| D03         | thyroid and other endocrine glands         |
| D04         | ill-defined, other secondary, and unspecified sites |
| D05         | lymphoid, hematopoietic, and related tissue |
| D06         | independent (primary) multiple sites        |
| D07         | oral cavity, esophagus, and stomach        |
| D09         | other and unspecified digestive organs     |
Supplement 2. Distribution of mean prescription dose of opioids during the prescription period

|                      | Control n=13,517 | Case I n=111 | Case II n=682 |
|----------------------|------------------|--------------|--------------|
| <30 mg/day           | 9,480 (70.1%)    | -            | -            |
| 30 - <60 mg/day      | 2,918 (21.6%)    | -            | -            |
| 60 - <90 mg/day      | 748 (5.5%)       | -            | -            |
| 90 - <120 mg/day     | 228 (1.7%)       | -            | -            |
| 120 - <200 mg/day    | 114 (0.8%)       | 79 (71.2%)   | 366 (53.7%)  |
| 200 - <300 mg/day    | 9 (0.1%)         | 14 (12.6%)   | 183 (26.8%)  |
| 300 - <400 mg/day    | 8 (0.1%)         | 9 (8.1%)     | 61 (8.9%)    |
| 400 - <500 mg/day    | 3 (0.0%)         | 1 (0.9%)     | 25 (3.7%)    |
| ≥500 mg/day          | 9 (0.1%)         | 8 (7.2%)     | 47 (6.9%)    |

*a Case group is defined by ≥120 mg/day of oral morphine equivalence
Supplement 3. Definition of comorbidities

| Comorbidities                        | Definition                                                                 |
|--------------------------------------|---------------------------------------------------------------------------|
| herpes zoster                        | ICD 10 code: B02, G53                                                    |
| osteoarthritis of knee               | ICD 10 code: M17                                                         |
| back pain                            | ICD 10 code: M54                                                         |
| spinal stenosis                      | ICD 10 code: M480                                                        |
| spondylosis                          | ICD 10 code: M47                                                         |
| other disorders of bone              | ICD 10 code: M89                                                         |
| alcohol dependence                   | ICD 10 code: F102                                                        |
| other psychoactive                   | ICD 10 code: F192                                                        |
| substance dependence                 | ICD 10 code: F20-F29                                                     |
| schizophrenia                        | ICD 10 code: F20-F29                                                     |
| mood disorders                        | ICD 10 code: F30-F39                                                     |
| anxiety                              | ICD 10 code: F40-F48                                                     |
| sleep disorders                      | ICD 10 code: F51                                                         |
| delirium due to known physiological condition | ICD 10 code: F05                                           |
| dementia                             | ICD 10 code: F01-F03                                                     |
| diabetes mellitus                    | ICD 10 code: E10-E14                                                     |
| hepatic disorder                     | ICD 10 code: K769 or patients with AST or ALT of 100 or more in the period from the date of first diagnosis of cancer to 365 days after the index date |
| chronic kidney disease               | ICD 10 code: M18 or patients with eGFR of less than 60 in the period from the date of first diagnosis of cancer to 365 days after the index date |
Supplement 4. Definition of analgesics other than opioids

| Analgesics other than opioids | ATC code | Generic name          |
|------------------------------|----------|-----------------------|
| Non-opioid analgesics        | B01C1    | Aspirin               |
|                              | M01A1    | Ibuprofen             |
|                              | M01A1    | Indomethacin          |
|                              | M01A1    | Etodolac              |
|                              | M01A1    | Diclofenac sodium     |
|                              | M01A1    | Naproxen              |
|                              | M01A1    | Flurbiprofen          |
|                              | M01A1    | Meloxicam             |
|                              | M01A1    | Loxoprofen sodium hydrate |
|                              | M01A3    | Celecoxib             |
|                              | N02B0    | Aspirin               |
|                              | N02B0    | Acetaminophen         |
| TCA                          | N06A9    | Amitriptyline hydrochloride |
|                              | N06A9    | Amoxapine             |
|                              | N06A9    | Imipramine hydrochloride |
|                              | N06A9    | Clomipramine hydrochloride |
|                              | N06A9    | Trimipramine maleate  |
|                              | N06A9    | Dosulepin hydrochloride |
|                              | N06A9    | Nortriptyline hydrochloride |
|                              | N06A9    | Lofepramine hydrochloride |
| SSRI                         | N06A4    | Sertraline hydrochloride |
|                              | N06A4    | escitalopram oxalate  |
|                              | N06A4    | Paroxetine hydrochloride hydrate |
|                              | N06A4    | Fluvoxamine maleate   |
| SNRI                         | N06A5    | Duloxetine hydrochloride |
|                              | N06A5    | Venlafaxine hydrochloride |
|                              | N06A5    | Milnacipran hydrochloride |
| Gabapentinoid                | N02B0    | Mirogabarine Besylate |
|                              | N03A0    | Pregabalin            |
| Antiepileptic                | N03A0    | Acetylphenetride      |
|                              | N03A0    | Ethosuximide          |
| ATC Code | Drug Name                                      |
|---------|-----------------------------------------------|
| N03A0   | Carbamazepine                                 |
| N03A0   | Gabapentin                                    |
| N03A0   | Gamma-Amino Butyric Acid                      |
| N03A0   | Clonazepam                                    |
| N03A0   | Clobazam                                      |
| N03A0   | Stilipentol                                   |
| N03A0   | Sulciam                                       |
| N03A0   | Zonisamide                                    |
| N03A0   | Topiramate                                    |
| N03A0   | Trimetadione                                  |
| N03A0   | Sodium valproate                              |
| N03A0   | Vigabatrin                                    |
| N03A0   | Phenytoin                                     |
| N03A0   | Phenytoin sodium                              |
| N03A0   | Phenytoin-Phenobarbital                      |
| N03A0   | Phenytoin-Phenobarbital Combination           |
| N03A0   | Phenobarbital sodium                          |
| N03A0   | Primidone                                     |
| N03A0   | Pregabalin                                    |
| N03A0   | Perampanel hydrate                            |
| N03A0   | Fosphenytoin sodium hydrate                   |
| N03A0   | Midazolam                                     |
| N03A0   | Lacosamide                                    |
| N03A0   | Lamotrigine                                    |
| N03A0   | Rufinamide                                    |
| N03A0   | Levetiracetam                                  |
| N03A0   | Lorazepam                                     |
| N03A0   | Diazepam                                      |
| N03A0   | Magnesium sulphate hydrate and dextrose       |
| C01B0   | Aplindin hydrochloride                         |
| C01B0   | Mexiletine hydrochloride                      |
| C01B0   | Lidocaine                                     |
| C01B0   | Lidocaine hydrochloride                       |
| C04A1   | Ifenprodil tartrate                           |
| N01A2   | Ketamine hydrochloride                        |

**Antiarrhythmic**

| ATC Code | Drug Name               |
|----------|-------------------------|

**NMDA receptor antagonist**
| ATC Code | Chemical Name                      |
|----------|-----------------------------------|
| N04A0    | Amantadine hydrochloride          |
| N07D9    | Memantine hydrochloride           |
| R05D1    | Dextromethorphan hydrobromide hydrate |
| M03B0    | Afroqualone                       |
| M03B0    | Eperisone hydrochloride           |
| M03B0    | Chlorfenecin carbamate            |
| M03B0    | Tizanidine hydrochloride          |
| M03B0    | Tolperisone hydrochloride         |
| M03B0    | Baclofen                          |
| M03B0    | Pridinol mesylate                 |
| M03B0    | Methocarbamol                     |
Supplement 5. Details of the diagnosis related to back pain

| Diagnosis                                | Control n=5,964 | Case I n=75 | Case II n=441 |
|-----------------------------------------|-----------------|-------------|---------------|
| Acute lower back pain                   | 190(3.2%)       | 1(1.3%)     | 8(1.8%)       |
| Pain of thoracic spine                  | 6(0.1%)         | 0(0.0%)     | 2(0.5%)       |
| Chest/back pain                         | 108(1.8%)       | 1(1.3%)     | 6(1.4%)       |
| Musculofascial lower back pain          | 43(0.7%)        | 0(0.0%)     | 5(1.1%)       |
| Cervicogenic headache                   | 2(0.0%)         | 0(0.0%)     | 0(0.0%)       |
| Cervical back pain                      | 4(0.1%)         | 0(0.0%)     | 0(0.0%)       |
| Cervical radiculopathy                  | 8(0.1%)         | 0(0.0%)     | 2(0.5%)       |
| Neck pain                               | 280(4.7%)       | 5(6.7%)     | 9(2.0%)       |
| Cervicobrachial neuralgia               | 3(0.1%)         | 0(0.0%)     | 0(0.0%)       |
| Nuchal pain                             | 3(0.1%)         | 0(0.0%)     | 0(0.0%)       |
| Lumbosciatic neuralgia syndrome         | 7(0.1%)         | 0(0.0%)     | 1(0.2%)       |
| Lower back pain                         | 5,440(91.2%)    | 70(93.3%)   | 409(92.7%)    |
| Lumbogluteal pain                       | 11(0.2%)        | 0(0.0%)     | 1(0.2%)       |
| Lumbar radiculitis                      | 8(0.1%)         | 0(0.0%)     | 2(0.5%)       |
| Lumboabdominal pain                     | 8(0.1%)         | 0(0.0%)     | 1(0.2%)       |
| Lower back pain of radicular origin     | 6(0.1%)         | 1(1.3%)     | 1(0.2%)       |
| Sciatic neuralgia                       | 96(1.6%)        | 0(0.0%)     | 14(3.2%)      |
| Radiculitis                             | 5(0.1%)         | 0(0.0%)     | 1(0.2%)       |
| Spinal radiculopathy                    | 2(0.0%)         | 0(0.0%)     | 0(0.0%)       |
| Spine pain                              | 1(0.0%)         | 0(0.0%)     | 0(0.0%)       |
| Hip pain                                | 79(1.3%)        | 2(2.7%)     | 12(2.7%)      |
| Back pain                               | 256(4.3%)       | 5(6.7%)     | 25(5.7%)      |
| Chronic lower back pain                 | 21(0.4%)        | 1(1.3%)     | 3(0.7%)       |