**Appendix Table 1.** ICD-9-CM Definitions for Potential Indications, Prescribing Cautions, and Prescription Medications

| Prescription Medications   |  |
|--|--|
| Variable   | ICD-9-CM codes   |
| Potential indication   |  |
| Anxiety disorders  | 300.0x; 300.2x; 300.3x; 308.x; 309.21; 309.81; 313.0x; 313.2x; 293.84; 799.21  |
| Sleep problems   | 307.4x; 327.0x; 327.3x; 327.4x; 327.5x; 327.8x; 780.50; 780.52; 780.55; 780.56; 780.58; 780.59   |
| Depressive disorders   | 296.2x; 296.3x; 300.4x; 309.1x; 311.x  |
| Bipolar disorder,<br>schizophrenia, other<br>psychotic disorders | 295.x; 296.0x; 296.1x; 296.4x; 296.5x; 296.6x; 296.7x; 296.8x; 293.81; 293.82; 297.x; 298.x  |
| Conduct/disruptive behavior disorders                            | 312.x; 313.81  |
| Epilepsy, convulsions  | 345.x; 780.3x  |
| Movement disorders, muscle spasm                                 | Cerebral palsy (343); tics (307.2x); muscular dystrophies and other myopathies (359.x); motor neuron diseases (335.x); movement disorders (332.x; 333.x); spasm of muscle/abnormal   |
|  | involuntary movements (728.85; 781.0x)   |
| Other uncommon   | Alcohol withdrawal (291.81; 291.0; 303.90–92); burning mouth syndrome (529.6); trigeminal neuralgia (350.1); Irritability/impulsiveness (799.22; 799.23)   |
| Injury   | 800–904; 910–957   |
| Musculoskeletal,<br>connective tissue<br>condition               | 710–739 [Subcategories: Spine curvature=737.x; Pain in joint/limb=719.4x, 729.5x; Back/neck pain=723.1x, 723.5x, 724.2x, 724.5x]   |
| Prescribing caution  | , <b>,</b>   |
| Drug-related disorders   | 292.x; 304.x; 305.2x-305.9x; 965.0x; 760.72; 760.73; 760.75; 779.5; 648.3x; 655.5x   |
| Alcohol-related disorder   | 291.1x-291.5x; 291.82; 291.89; 291.9x; 303.0x; 303.93; 305.0x; 980.0x; E860.0; V11.3; 760.71; 790.3x   |
| Suicidality  | V62.84; E950–E959  |
| Poisoning  | 960–964.x; 965.1x–965.9x; 966–979.x; 980.1x–980.9x; 981–<br>989.x; E850–E858; E860.1–E860.9; E861–E869; E980; E981;<br>E982  |
| Sleep apnea,<br>hypersomnia                                      | 327.1x; 327.2x; 780.51; 780.53; 780.54; 780.57   |
| Respiratory failure,   | 518.81; 518.83; 518.84; 799.02 (Note: diagnoses on date of   |
| hypoxemia  | benzodiazepine initiation excluded)  |
| Opioid prescription  | Alfentanil, buprenorphine, butorphanol, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, nalbuphine, oxycodone, oxymorphone, pentazocine, propoxyphene, remifentanil, sufentanil, tapentadol, tramadol |
| Psychotropic prescription  |  |

| SSRI                 | Fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram, vilazodone   |
|----------------------|---|
| Other antidepressant | Desvenlafaxine, duloxetine, levomilnacipran, milnacipran, venlafaxine, amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline, protriptyline, trimipramine, maprotiline, bupropion, isocarboxazid, phenelzine, tranylcypromine, selegiline, rasagiline, vortioxetine, nefazodone, trazodone, mirtazapine |
| Stimulant            | Amphetamine, dextroamphetamine, dexmethylphenidate, lisdexamfetamine, metamfetamine, methylphenidate  |
| Hypnotic             | Zolpidem, zaleplon, eszopiclone, suvorexant, ramelteon, tasimelteon, butabarbital, secobarbital, pentobarbital  |
| Antipsychotic        | Aripiprazole, asenapine, cariprazine, chlorpromazine, clozapine, fluphenazine, haloperidol, iloperidone, loxapine, lurasidone, molindone, olanzapine, paliperidone, perphenazine, pimozide, quetiapine, risperidone, thioridazine, thiothixene, trifluoperazine, ziprasidone  |

SSRI, selective serotonin reuptake inhibitor.

**Appendix Table 2.** Initial Benzodiazepine and Days' Supply Dispensed to Children and Adolescents by Potential Benzodiazepine Indication<sup>a</sup>

| Potential indication,   | N      | Initial days' supply |                       | Long-              | Initial BZD (four most common) |                  |                   |                   |
|---|--------|----------------------|-----------------------|--------------------|--------------------------------|------------------|-------------------|-------------------|
| prior 30 days   |        | Median<br>(IQR)      | >2<br>weeks,<br>row % | acting<br>BZD, row | Diazepam,<br>row %             | Lorazepam, row % | Clonazepam, row % | Alprazolam, row % |
| Bipolar disorder,<br>schizophrenia, other<br>psychotic disorder | 3,415  | 30 (10–30)           | 72                    | 45                 | 5                              | 36               | 40                | 14                |
| Sleep problem   | 2,680  | 30 (10–30)           | 71                    | 44                 | 8                              | 24               | 35                | 20                |
| Depression  | 12,592 | 25 (10–30)           | 67                    | 42                 | 5                              | 30               | 36                | 25                |
| Conduct/disruptive behavior disorder                            | 1,877  | 25 (10–30)           | 65                    | 43                 | 9                              | 37               | 34                | 16                |
| Anxiety disorder  | 23,592 | 15 (7–30)            | 57                    | 37                 | 6                              | 31               | 30                | 30                |
| Epilepsy, convulsions   | 5,372  | 15 (6–30)            | 50                    | 72                 | 16                             | 24               | 42                | 3                 |
| Movement disorders, muscle spasm                                | 5,075  | 10 (5–30)            | 40                    | 78                 | 52                             | 16               | 22                | 6                 |
| Musculoskeletal condition                                       | 19,641 | 7 (5–15)             | 27                    | 77                 | 67                             | 13               | 9                 | 8                 |
| Injury  | 10,707 | 7 (5–15)             | 26                    | 75                 | 65                             | 14               | 10                | 9                 |
| No potential indication   | 28,563 | 10 (5–30)            | 38                    | 47                 | 28                             | 26               | 17                | 19                |

<sup>&</sup>lt;sup>a</sup>Children and adolescents can have multiple potential indications; potential indications based on diagnoses in the prior 30 days, and on the day of, benzodiazepine initiation; potential indications displayed by descending longest days' supply; cohort is restricted to children and adolescents initiating with at least a 3 day supply.

BZD, benzodiazepine.

<sup>&</sup>lt;sup>b</sup>Other, uncommon category not displayed due to low count (n=145, days' supply median=15, IQR=7–30).

**Appendix Table 3.** Sensitivity Analysis: Children and Adolescent Benzodiazepine Initiators Without a Recent Inpatient Admission<sup>a</sup>

| Variable  | Children, %<br>N=20,187 | Adolescents, %<br>N=53,727 |
|---|-------------------------|----------------------------|
| Age at benzodiazepine start, median (IQR)                               | 10.0 (7.0–11.0)         | 16.0 (15.0–17.0)           |
| Female  | 45.6                    | 60.8                       |
| Potential indication, diagnoses prior 30 days <sup>b</sup>              |                         |                            |
| Any potential indication  | 40.9                    | 51.3                       |
| Any potential indication including injury and musculoskeletal condition | 57.9                    | 65.9                       |
| Mental health potential indication                                      | 25.1                    | 46.2                       |
| Anxiety disorder  | 18.9                    | 32.6                       |
| Sleep problems  | 3.0                     | 3.4                        |
| Bipolar disorder, schizophrenia, and other psychotic disorders          | 1.7                     | 3.7                        |
| Conduct/disruptive behavior disorders                                   | 2.7                     | 1.6                        |
| Depression  | 3.5                     | 18.2                       |
| Epilepsy, convulsions   | 11.6                    | 3.4                        |
| Movement disorders, muscle spasm  | 8.3                     | 3.9                        |
| Injury  | 10.8                    | 11.6                       |
| Musculoskeletal, connective tissue condition <sup>b</sup>               | 19.5                    | 18.4                       |
| Prescribing cautions  |                         |                            |
| Drug-related disorder   | 0.3                     | 3.2                        |
| Alcohol-related disorder  | 0.1                     | 0.9                        |
| Suicidality   | 0.6                     | 3.5                        |
| Poisoning   | 0.9                     | 2.1                        |
| Sleep apnea; hyposomnia   | 2.6                     | 1.3                        |
| Respiratory failure; hypoxia  | 1.2                     | 0.3                        |
| Opioid prescription, same date  | 10.0                    | 12.2                       |
| Opioid prescription, prior 30 days                                      | 12.9                    | 16.4                       |
| >10 days supplied   | 2.6                     | 2.3                        |
| Other characteristics <sup>b</sup>                                      |                         |                            |
| Mental health provider contact, prior 30 days                           | 19.4                    | 27.6                       |
| General provider contact, prior 30 days                                 | 46.4                    | 49.3                       |
| Specialist provider contact, prior 30 days                              | 28.2                    | 21.6                       |
| Neurology   | 8.5                     | 3.9                        |
| Surgery, radiology, anesthesiology                                      | 18.3                    | 16.9                       |
| Pediatrician specialty, other   | 7.3                     | 4.0                        |
| Complex chronic condition   | 4.4                     | 1.7                        |

<sup>&</sup>lt;sup>a</sup>Excluded=children and adolescents initiating benzodiazepines with a psychiatric or non-psychiatric-related inpatient admission in 30 days before benzodiazepine initiation.

SSRI, selective serotonin reuptake inhibitor.

<sup>&</sup>lt;sup>b</sup>Children and adolescent initiators, respectively, with: other uncommon indication (0.1%, 0.1%); Musculoskeletal sub-categories: spine curvature (0.9%, 0.9%); pain in limb/join (5.1%, 6.6%); pain in neck/back (7.0%, 6.6%); Mental health diagnosis (38.0%, 53.7%); Selected psychotropic prescriptions, prior 30 days: SSRIs (16.0%, 30.5%), other antidepressant (3.5%, 8.9%), stimulant (10.8%, 9.5%), antipsychotic (8.0%; 7.4%).

**Appendix Figure 1.** Potential indications in children and adolescents initiating prescription benzodiazepine treatment stratified by sex.

