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ORIGINAL RESEARCH

# Psychotropic Medication Use During Inpatient Rehabilitation for Traumatic Brain Injury

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**Abstract**

**Objective:** To describe psychotropic medication administration patterns during inpatient rehabilitation for traumatic brain injury (TBI) and their relation to patient preinjury and injury characteristics.

**Design:** Prospective observational cohort.

**Setting:** Multiple acute inpatient rehabilitation units or hospitals.

**Participants:** Individuals with TBI (N = 2130; complicated mild, moderate, or severe) admitted for inpatient rehabilitation.

**Interventions:** Not applicable.

**Main Outcome Measures:** Not applicable.

**Results:** Most frequently administered were narcotic analgesics (72% of sample), followed by antidepressants (67%), anticonvulsants (47%), anxiolytics (33%), hypnotics (30%), stimulants (28%), antipsychotics (25%), antiparkinson agents (25%), and miscellaneous psychotropics (18%). The psychotropic agents studied were administered to 95% of the sample, with 8.5% receiving only 1 and 31.8% receiving ≥6. Degree of psychotropic medication administration varied widely between sites. Univariate analyses indicated younger patients were more likely to receive anxiolytics, antidepressants, antiparkinson agents, stimulants, antipsychotics, and narcotic analgesics, whereas those older were more likely to receive anticonvulsants and miscellaneous psychotropics. Men were more likely to receive antipsychotics. All medication classes were less likely administered to Asians and more likely administered to those with more severe functional impairment. Use of anticonvulsants was associated with having seizures at some point during acute care or rehabilitation stays. Narcotic analgesics were more likely for those with history of drug abuse, history of anxiety and depression (premorbid or during acute care), and severe pain during rehabilitation. Psychotropic medication administration increased rather than decreased during the course of inpatient rehabilitation in each of the medication categories except for narcotics. This observation was also true for medication administration within admission functional levels (defined by cognitive FIM scores), except for those with higher admission FIM cognitive scores.

**Conclusions:** Many psychotropic medications are used during inpatient rehabilitation. In general, lower admission FIM cognitive score groups were administered more of the medications under investigation compared with those with higher cognitive function at admission. Considerable site variation existed regarding medications administered. The current investigation provides baseline data for future studies of effectiveness.

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Individuals with traumatic brain injury (TBI) frequently present to acute inpatient rehabilitation facilities with pain, hypoarousal, sleep dysregulation, behavioral dysregulation, spasticity, confusion, slowed cognitive processing, impaired memory, and affective disorders prompting prescription of multiple psychotropic

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medications.[1] Some of these medications are aimed at controlling behaviors to prevent harm and allow safer and more effective management of the patient (eg, use of stimulants, benzodiazepine, and antipsychotic agents to control agitation). Other medication uses are aimed at preventing comorbidities (eg, seizures), and some are aimed at enhancing function (eg, sleep medications, stimulants, antiparkinson agents).[2]

On admission and throughout the rehabilitation stay, the rehabilitation physician typically reviews prescribed medications to continually reassess the patient's needs. This includes discontinuing medications that no longer appear necessary or may cause an adverse response and adding other agents as deemed necessary. There is sparse literature to guide such clinical decision-making, and there are no medications that are currently approved by the U.S. Food and Drug Administration for the treatment of TBI. Additionally, the small body of published research is commonly limited by scientific rigor, such as lack of controlled trials, nonblinded prescribers, lack of information regarding injury, limited information on relevant data (eg, severity of injury, time of injury to treatment), mixed brain injury samples, and small sample sizes. Evidence of medication benefit and safety is usually extrapolated from therapeutic trials targeting common post-TBI conditions that also occur in other patient populations. An example would be the use of antipsychotic agents studied in patient populations other than brain injury and settings other than acute inpatient rehabilitation. There is a small but growing literature body regarding which pharmacologic agents may be helpful in the acute rehabilitation setting for persons who sustain TBI. For example, a randomized, placebo-controlled trial of 184 patients with TBI in rehabilitation in a vegetative state or minimally conscious state showed that amantadine was more effective than placebo in accelerating the rate of functional recovery.[3]

Various agents commonly used to manage the effects of TBI may cause adverse effects on health, function, and treatment efficiency.[4-10] For example, a retrospective review of 182 consecutive patients with moderate-to-severe TBI revealed commonly prescribed neuroleptics were associated with 7 days longer of posttraumatic amnesia (PTA).[1] In a study of individuals with TBI undergoing residential treatment, polypharmacy and use of anticholinergic medications were associated with an increased risk of falls.[11]

The degree to which psychotropic medications are used early after TBI during the course of inpatient rehabilitation is unknown. Use of psychotropic medications late after TBI was evaluated in a retrospective cohort study of 306 moderate-to-severe TBI survivors who had all been discharged from a TBI rehabilitation unit and were tracked up to 24 years postinjury. This study found that at follow-up, 58.9% were currently prescribed at least 1 medication. On average, persons with TBI were prescribed 2.64±2.14 medications (range, 1−12). The most prescribed medication types were anticonvulsants (25.8%), followed by antidepressants (8.2%), analgesics (8.2%), and anxiolytics (5.9%).[12]

Because of a lack of evidence on medication effects in patients with TBI, medication management during acute rehabilitation is driven largely by a patient's clinical presentation and physician subjective experience or preferences. Consequently, highly variable prescribing practices exist.[2,13] There is significant need to study physicians' medication administration patterns during acute TBI rehabilitation. Medication pattern data could then be used as the basis for future research. Specifically, such data could help identify commonly used types of medicine that would benefit from effectiveness analyses, inform research design (including sample size determination), and identify the degree to which sociodemographics, injury severity, and other potential confounds (eg, time from injury to rehabilitation, medical comorbidities, function, insomnia, agitation) would need to be addressed.

The Traumatic Brain Injury−Practice Based Evidence (TBI-PBE) project provides a unique opportunity to describe patterns of psychotropic medication administration at specialized inpatient brain injury rehabilitation units in the United States and Canada, including the medication agents prescribed, if medications were prescribed as the occasion arises (as needed) (PRN) or as scheduled, and timing of medication initiation and discontinuation across the course of rehabilitation. The TBI-PBE data also allow for evaluation of the relation between medication prescription and patient demographic, injury, medical, and function.

*List of abbreviations:*

| | |
|---|---|
| **AChEI** | **acetylcholinesterase inhibitor** |
| **CSI** | **Comprehensive Severity Index** |
| **PRN** | **as the occasion arises (as needed)** |
| **PTA** | **posttraumatic amnesia** |
| **RLOS** | **rehabilitation length of stay** |
| **SARI** | **serotonin antagonist and reuptake inhibitor** |
| **TBI** | **traumatic brain injury** |
| **TBI-PBE** | **Traumatic Brain Injury−Practice Based Evidence** |

# Methods

## Study design, study sites, and participants

The TBI-PBE Project is a 5-year, multicenter investigation of the TBI inpatient rehabilitation process.[14] A total of 2130 patients who received acute inpatient rehabilitation were enrolled in the project and used for the current study. The project sites included 10 inpatient rehabilitation facilities: 9 in the United States and 1 in Canada. The study was approved by the local institutional review board at each study site. Inclusion criteria included the following: participant age of ≥14 years, informed consent from participant or their parent/guardian, and admission to the facility's brain injury unit for initial rehabilitation after TBI.

## Variables and data collection

### Collection and classification of medications

Medication data were collected either through manual chart abstraction or electronic data download, depending on the site and availability and dependability of electronic data. Only those medications actually administered were recorded. Medications ordered but not given for any reason were not recorded. As customary during inpatient rehabilitation, medications were administered and recorded by nursing staff. Also per routine practice, a rehabilitation physician wrote the admission medication orders within minutes to hours of the patient's arrival to the inpatient rehabilitation unit and performed history and physical examination within 24 hours.

Common drug classification schemes vary, based on factors such as the chemical type of the active ingredient (eg, benzodiazepines), presumed mechanisms of action (eg, serotonin reuptake

inhibitor), or clinical indications for use (eg, antidepressant). Medications were grouped primarily by common clinical usage/purpose and then by general mechanism of action. We also were aware that many drugs could be classified into >1 class (eg, divalproex sodium could be classified as an anticonvulsant and a mood stabilizer). For the purpose of this study, medications were classified in only 1 category. The classification scheme is outlined in table 1. Patients may have been administered medications from multiple classes or >1 agent within a class, simultaneously or successively.

The medications studied included the following: anxiolytic agents, anticonvulsants, antidepressants, antiparkinson agents, stimulants, antipsychotics, hypnotics, miscellaneous psychotropics, and narcotic analgesics. These agents were selected among the many medications because of the need to focus the study, commonality of use in acute brain injury care, and the agent's use specifically for their central-acting property. Other psychotropic agents exist that were not studied (eg, some centrally acting antihypertensives, gastrointestinal agents).

### Descriptive variables

The variables for this study were chosen by the study investigators and clinicians at the onset of the project based on their clinical impressions and literature review of factors relevant to brain injury care and outcome. These data were obtained through medical record abstraction and interview with the study participants and their close others (proxy). Variables were chosen to represent patient characteristics prior to injury, postinjury before admission to rehabilitation, and during inpatient rehabilitation.

### Premorbid variables

Premorbid variables studied for association with medication use included age (both continuous and categorical), sex, race, history of psychosis/schizophrenia/bipolar disorder, and history of alcohol or drug abuse.

### Patient injury and medical data

Patient injury and medical data were abstracted from patient medical records by trained data collectors. Several variables were used to describe injury severity, including postresuscitation Glasgow Coma Scale score in the emergency department, duration of PTA, and time from injury to rehabilitation admission. Any mention of presence of depression or anxiety in the medical record during acute care or at rehabilitation admission was recorded representing problems in this area premorbidly or during acute care. The extent and severity of medical illness during the rehabilitation stay was captured using the maximum Comprehensive Severity Index (CSI) score. The CSI is derived by scoring the extent of deviation from normative physiological status for each medical complication and comorbidity present, with a higher CSI score denoting greater medical severity.[15] A brain injury CSI subscore was used to establish the severity of central nervous system illness, whereas a nonbrain injury CSI subscore established severity of illness of all other injuries, existing chronic disorders, complications, and comorbidities. The CSI score used for this study represented the maximum CSI score for the entire course of rehabilitation.[14] Functional status and need for assistance were measured at rehabilitation admission by the FIM. The FIM cognitive and motor scale scores were Rasch-transformed to a ratio scale using scores from 0 to 100.[14,16]

### Rehabilitation variables

Rehabilitation variables included the following: presence of seizures at any point up to rehabilitation discharge (premorbid, during acute care, during rehabilitation); percentage of rehabilitation days with <5 hours of sleep between the hours of 9 PM and 6 AM; percentage of rehabilitation stay agitated (defined as 6 shifts with Agitated Behavior Scale scores >21 out of twelve 4-hour shifts)[17]; and average level of effort over the stay for physical therapy, occupational therapy, and speech therapy, combined.[18] Severity of pain was operationalized as percentage of the rehabilitation stay with a patient-reported pain score of ≥7 (out of a possible score of 10, which was the worst pain).[19]

## Data processing and analysis

### Description of medication administration during course of rehabilitation

Percentages were used to portray the frequency of psychotropic medication administration for each pharmaceutical class during rehabilitation.

### Comparison by cognitive function at rehabilitation admission

Five relatively homogenous subgroups were created based on admission FIM cognitive scores to stratify the impact of patients' cognitive impairments on outcomes and facilitate between-group comparisons of medications administered.[14] The admission FIM cognitive score categories used were <6, 7 to 10, 11 to 15, 16 to 20, and >21.

### Factors related to medications administered

Data were analyzed to determine patient characteristics that may differentiate whether medications in each pharmaceutical class were either administered or not administered. Medication administration patterns were also compared across treatment sites (details will be subsequently discussed). Categorical variables with >2 categories (eg, site, age, race/ethnicity) were evaluated using the chi-square test; categorical variables with 2 categories (eg, sex) were evaluated with the Fisher exact test. Continuous variables (eg, brain injury and nonbrain injury CSI) were evaluated using the independent samples $t$ test. To minimize type I error, only differences reaching an $\alpha$ level of $P<.001$ were considered significant. Correction for multiple comparisons was not performed because of the exploratory nature of this descriptive article.

### Calculation of rehabilitation weeks

To study the timing of medication initiation and discontinuation across the course of rehabilitation we depicted medication administration by week of stay in rehabilitation. All patients with a rehabilitation length of stay (RLOS) of ≤8 days were considered to have only 1 admission week. All others have an admission (week 1) and discharge week, at a minimum. Patients with an RLOS of 9 to 15 days have a 2-week stay; patients with an RLOS of 16 and 17 days have a 3-week stay (with the admission week comprised of only 6d). All patients with an RLOS ≥18 days were classified as follows: 18 to 22 days was a 3-week stay, 23 to 29 was a 4-week stay, 30 to 36 days was a 5-week stay, and so forth. There were no weeks <4 days, and none were >8 weeks. For RLOS with remainders of 1 when divided by 7 (eg, 22, 29), the extra day was added to the discharge week to create an 8-day week.

**Table 1** Classification for the psychoactive medications administered

| Major Drug Class and General Mechanism | Pharmacological Agents Received* | Total No. of Patients Receiving Agent† |
|---|---|---|
| Anxiolytic | | |
| GABA-A agonist | Lorazepam (478; 68), clonazepam (85; 12), alprazolam (67; 10), diazepam (66; 9), chlordiazepoxide (5; <1) | 701 |
| H-1 receptor antagonist | Hydroxyzine (21; 100) | 21 |
| Other | Buspirone (151; 100) | 151 |
| Anticonvulsant | | |
| Calcium channel antagonist | Levetiracetam (440; 61), gabapentin (219; 30), pregabalin (65; 9) | 724 |
| GABA-A agonist | Tiagabine (4; 100) | 4 |
| Sodium channel antagonist | Valproic acid (239; 39), phenytoin (229; 37), carbamazepine (56; 9), topiramate (38; 6), lamotrigine (23; 4), oxcarbazepine (13; 2), fosphenytoin (12; 2) primidone (3; <1), zonisamide (2; <1) | 612 |
| Other | Lacosamide (3; 100) | 3 |
| Antidepressant | | |
| Norepinephrine-dopamine reuptake inhibitor | Bupropion (30; 100) | 30 |
| NaSSA | Mirtazapine (70; 100) | 70 |
| SARI | Trazodone (1124; 100) | 1124 |
| Serotonin and norepinephrine reuptake inhibitor | Duloxetine (54; 52), venlafaxine (45; 44), milnacipran (4; 4) | 103 |
| Selective serotonin reuptake inhibitor | Paroxetine (44; 8), fluoxetine (37; 6) | 81 |
| TCA—secondary amine | Nortriptyline (34; 92), desipramine (3; 8) | 37 |
| TCA—tertiary amine | Amitriptyline (62; 95), doxepin (3; 5) | 65 |
| Antiparkinson | | |
| Catechol-O-methyltransferase inhibitor | Entacapone (1; 100) | 1 |
| Dopamine agonist | Bromocriptine (190; 95), pramipexole (7; 3), ropinirole (4; 2) | 201 |
| Monoamine oxidase inhibitor | Benzatropine (15; 79), rasagiline (2; 11), selegiline (2; 11) | 19 |
| NMDA antagonist | Amantadine (361; 100) | 361 |
| Other | Carbidopa plus levodopa (28; 88), levodopa (4; 13) | 32 |
| Stimulant | | |
| Norepinephrine agonist | Atomoxetine (56; 100) | 56 |
| Norepinephrine-dopamine-5HT agonist | Sulfate plus dextroamphetamine saccharate plus dextroamphetamine sulfate (24; 5), amphetamine plus dextroamphetamine (6; 1), dextroamphetamine (3; <1) | 490 |
| Other | Modafinil (117; 96), armodafinil (6; 4) | 123 |
| Antipsychotic | | |
| First generation/typical | Haloperidol (36; 66%), prochlorperazine (13; 24%), chlorpromazine (6; 11%) | 55 |
| Second generation/atypical | Quetiapine (307; 48), risperidone (119; 19), olanzapine (93; 15), ziprasidone (92; 14), aripiprazole (25; 4), paliperidone (1; <1) | 637 |
| Hypnotic | | |
| Benzodiazepine GABA-A agonist | Temazepam (63; 62), midazolam (38; 38) | 101 |
| Nonbenzodiazepine GABA-A agonist | Zolpidem (482; 88), eszopiclone (62; 11), zaleplon (3; <1) | 547 |
| Melatonin agonist | Ramelton (13; 100) | 13 |
| Other | Chloral hydrate (36; 57), propofol (26; 41), phenobarbital (1; 2) | 63 |
| Narcotic analgesic | | |
| Narcotic | Oxycodone (864; 37), APAP plus hydrocodone (688; 30), morphine (205; 9), fentanyl (145; 6), tramadol (142; 6), hydromorphone (85; 4), propoxyphene N plus APAP (84; 4), codeine (48; 2), methadone (44; 2), APAP plus codeine (14; <1), meperidine (4; <1), buprenorphine (4; <1), propoxyphene N (4; <1) | 2234 |
| Miscellaneous psychotropic | | |
| AChEI | Donepezil (178; 95), rivastigmine (6; 3), physostigmine salicylate (3; 2) | 187 |
| NMDA antagonist | Memantine (29; 100) | 29 |
| Other | Nicotine (204; 98), interferon beta-1a (2; <1), glatiramer acetate (1; <1), varenicline (1; <1) | 208 |

Abbreviations: APAP, acetaminophen; GABA-A, gamma-aminobutyric acid-A; NaSSA, noradrenergic and specific serotonergic antidepressant; NMDA, N-methyl-D-aspartate; TCA, tricyclic antidepressant.

* Values are (number of patients who received agent among sample of 2130 with medication data; % of patients who received the agent among the other agents in that mechanism within that classification).

† Patients may receive >1 agent within a mechanism.

**Table 2** Summary information on psychoactive medications administered during rehabilitation, by pharmaceutical category and level of functional cognition

| Pharmaceutical Category | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anxiolytic | Overall | 2130 | 33 | 19 | 19 | 11 | 23 | 17 | 12 | 56 | 58 | 37 | 53 | 10 |
| | Adm FIM cog ≤6 | 339 | 48 | 24 | 26 | 14 | 31 | 21 | 18 | 50 | 50 | 40 | 45 | 14 |
| | Adm FIM cog 7—10 | 374 | 44 | 23 | 26 | 12 | 32 | 19 | 14 | 53 | 52 | 37 | 55 | 7 |
| | Adm FIM cog 11—15 | 495 | 31 | 18 | 18 | 11 | 22 | 17 | 13 | 60 | 67 | 36 | 57 | 7 |
| | Adm FIM cog 16—20 | 408 | 28 | 20 | 17 | 13 | 20 | 13 | 9 | 62 | 73 | 33 | 56 | 11 |
| | Adm FIM cog ≥21 | 504 | 20 | 13 | 12 | 7 | 14 | 12 | 10 | 60 | 65 | 39 | 50 | 11 |
| Anticonvulsant | Overall | 2130 | 47 | 35 | 39 | 28 | 43 | 23 | 17 | 81 | 100 | 6 | 76 | 19 |
| | Adm FIM cog ≤6 | 339 | 50 | 32 | 40 | 25 | 48 | 35 | 28 | 76 | 93 | 8 | 71 | 21 |
| | Adm FIM cog 7—10 | 374 | 52 | 34 | 42 | 26 | 48 | 27 | 23 | 77 | 94 | 3 | 85 | 12 |
| | Adm FIM cog 11—15 | 495 | 46 | 34 | 39 | 28 | 44 | 22 | 18 | 83 | 100 | 4 | 80 | 16 |
| | Adm FIM cog 16—20 | 408 | 46 | 38 | 41 | 33 | 43 | 19 | 15 | 87 | 100 | 4 | 73 | 22 |
| | Adm FIM cog ≥21 | 504 | 41 | 37 | 32 | 28 | 36 | 13 | 12 | 83 | 100 | 10 | 67 | 24 |
| Antidepressant | Overall | 2130 | 67 | 44 | 55 | 37 | 61 | 23 | 18 | 78 | 93 | 27 | 60 | 13 |
| | Adm FIM cog ≤6 | 339 | 77 | 47 | 64 | 40 | 73 | 34 | 29 | 79 | 94 | 23 | 62 | 15 |
| | Adm FIM cog 7—10 | 374 | 76 | 48 | 63 | 39 | 72 | 26 | 22 | 78 | 90 | 25 | 65 | 10 |
| | Adm FIM cog 11—15 | 495 | 66 | 46 | 54 | 38 | 60 | 21 | 19 | 80 | 95 | 30 | 57 | 13 |
| | Adm FIM cog 16—20 | 408 | 69 | 49 | 58 | 42 | 62 | 17 | 14 | 78 | 95 | 28 | 57 | 15 |
| | Adm FIM cog ≥21 | 504 | 53 | 35 | 41 | 28 | 42 | 15 | 12 | 74 | 90 | 30 | 57 | 13 |
| Antiparkinson | Overall | 2130 | 25 | 11 | 20 | 8 | 23 | 25 | 21 | 73 | 83 | 3 | 83 | 14 |
| | Adm FIM cog ≤6 | 339 | 53 | 24 | 40 | 17 | 49 | 30 | 26 | 70 | 79 | 4 | 84 | 12 |
| | Adm FIM cog 7—10 | 374 | 40 | 18 | 31 | 13 | 36 | 25 | 22 | 71 | 85 | 1 | 87 | 12 |
| | Adm FIM cog 11—15 | 495 | 21 | 8 | 19 | 7 | 20 | 24 | 19 | 78 | 86 | 2 | 82 | 15 |
| | Adm FIM cog 16—20 | 408 | 15 | 4 | 12 | 4 | 13 | 16 | 14 | 71 | 75 | 5 | 72 | 23 |
| | Adm FIM cog ≥21 | 504 | 6 | 4 | 6 | 3 | 5 | 14 | 14 | 80 | 100 | 5 | 73 | 23 |
| Antipsychotic | Overall | 2130 | 25 | 16 | 15 | 10 | 21 | 20 | 15 | 65 | 75 | 23 | 62 | 15 |
| | Adm FIM cog ≤6 | 339 | 38 | 18 | 23 | 10 | 34 | 27 | 20 | 57 | 55 | 29 | 49 | 22 |
| | Adm FIM cog 7—10 | 374 | 34 | 21 | 23 | 13 | 30 | 21 | 17 | 66 | 78 | 24 | 61 | 15 |
| | Adm FIM cog 11—15 | 495 | 28 | 21 | 18 | 13 | 23 | 18 | 15 | 71 | 89 | 18 | 74 | 8 |
| | Adm FIM cog 16—20 | 408 | 22 | 16 | 11 | 7 | 18 | 15 | 13 | 63 | 75 | 17 | 71 | 12 |
| | Adm FIM cog ≥21 | 504 | 10 | 8 | 6 | 5 | 7 | 12 | 9 | 65 | 70 | 33 | 50 | 16 |
| Hypnotic | Overall | 2130 | 30 | 14 | 20 | 10 | 23 | 18 | 13 | 60 | 67 | 48 | 42 | 10 |
| | Adm FIM cog ≤6 | 339 | 36 | 14 | 23 | 9 | 29 | 24 | 21 | 57 | 58 | 34 | 51 | 16 |
| | Adm FIM cog 7—10 | 374 | 37 | 17 | 26 | 12 | 31 | 22 | 18 | 62 | 70 | 41 | 50 | 9 |
| | Adm FIM cog 11—15 | 495 | 31 | 15 | 20 | 10 | 25 | 18 | 14 | 61 | 68 | 47 | 46 | 7 |
| | Adm FIM cog 16—20 | 408 | 25 | 13 | 16 | 8 | 16 | 11 | 9 | 57 | 64 | 55 | 35 | 9 |
| | Adm FIM cog ≥21 | 504 | 24 | 13 | 16 | 9 | 17 | 11 | 8 | 62 | 70 | 68 | 23 | 10 |

(*continued on next page*)

**Table 2** (*continued*)

| Pharmaceutical Category | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Narcotic analgesic | Overall | 2130 | 72 | 55 | 45 | 36 | 59 | 16 | 13 | 65 | 77 | 63 | 26 | 11 |
| | Adm FIM cog ≤6 | 339 | 71 | 50 | 35 | 26 | 59 | 21 | 17 | 56 | 51 | 63 | 25 | 12 |
| | Adm FIM cog 7—10 | 374 | 74 | 50 | 40 | 29 | 60 | 18 | 14 | 57 | 59 | 61 | 30 | 9 |
| | Adm FIM cog 11—15 | 495 | 73 | 56 | 42 | 35 | 59 | 16 | 13 | 62 | 70 | 64 | 26 | 10 |
| | Adm FIM cog 16—20 | 408 | 75 | 60 | 51 | 43 | 60 | 14 | 12 | 69 | 90 | 57 | 32 | 12 |
| | Adm FIM cog ≥21 | 504 | 69 | 59 | 52 | 46 | 58 | 14 | 11 | 78 | 100 | 69 | 19 | 12 |
| Miscellaneous psychotropic | Overall | 2130 | 18 | 8 | 15 | 6 | 16 | 19 | 15 | 69 | 75 | 9 | 78 | 13 |
| | Adm FIM cog ≤6 | 339 | 24 | 4 | 22 | 3 | 23 | 26 | 21 | 58 | 59 | 16 | 76 | 8 |
| | Adm FIM cog 7—10 | 374 | 19 | 7 | 14 | 5 | 17 | 21 | 17 | 65 | 68 | 10 | 77 | 13 |
| | Adm FIM cog 11—15 | 495 | 21 | 10 | 17 | 8 | 20 | 17 | 16 | 73 | 81 | 4 | 84 | 12 |
| | Adm FIM cog 16—20 | 408 | 19 | 12 | 16 | 9 | 17 | 16 | 14 | 75 | 90 | 5 | 78 | 17 |
| | Adm FIM cog ≥21 | 504 | 10 | 7 | 7 | 6 | 8 | 13 | 9 | 72 | 98 | 14 | 69 | 18 |
| Stimulant | Overall | 2130 | 28 | 7 | 22 | 6 | 26 | 23 | 18 | 66 | 72 | 5 | 83 | 12 |
| | Adm FIM cog ≤6 | 339 | 57 | 16 | 41 | 12 | 54 | 29 | 27 | 67 | 75 | 4 | 79 | 17 |
| | Adm FIM cog 7—10 | 374 | 44 | 10 | 36 | 9 | 43 | 25 | 22 | 68 | 78 | 3 | 89 | 8 |
| | Adm FIM cog 11—15 | 495 | 25 | 5 | 20 | 4 | 23 | 19 | 16 | 63 | 64 | 5 | 84 | 11 |
| | Adm FIM cog 16—20 | 408 | 15 | 5 | 12 | 4 | 13 | 13 | 11 | 65 | 67 | 9 | 78 | 14 |
| | Adm FIM cog ≥21 | 504 | 8 | 2 | 7 | 2 | 6 | 11 | 9 | 64 | 64 | 10 | 79 | 10 |

Abbreviation: Adm FIM cog, admission FIM cognitive score.

* Ten patients were excluded because of missing admission FIM cognitive scores.

**Table 3** Sample size by week and percentage with psychoactive medication administration by pharmaceutical class, week of rehabilitation, and level of cognitive function at admission

| Pharmaceutical Class | FIM Cognitive Score at Admission | Received Week 1 | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Sample size by week (n)* | Overall | 2130 | 2008 | 1551 | 1065 | 707 | 482 | 339 | 215 | 153 |
| | Adm FIM cog ≤6 | 339 | 333 | 323 | 288 | 223 | 160 | 107 | 79 | 59 |
| | Adm FIM cog 7—10 | 374 | 371 | 337 | 266 | 185 | 121 | 90 | 56 | 34 |
| | Adm FIM cog 11—15 | 495 | 482 | 387 | 236 | 127 | 73 | 48 | 30 | 27 |
| | Adm FIM cog 16—20 | 408 | 381 | 253 | 126 | 74 | 50 | 42 | 24 | 17 |
| | Adm FIM cog ≥21 | 504 | 432 | 242 | 140 | 91 | 71 | 47 | 23 | 16 |
| Anxiolytic (%) | Overall | 24 | 22 | 23 | 23 | 26 | 28 | 30 | 32 | 31 |
| | Adm FIM cog ≤6 | 31 | 30 | 29 | 30 | 30 | 29 | 30 | 33 | 27 |
| | Adm FIM cog 7—10 | 30 | 27 | 27 | 26 | 30 | 35 | 40 | 41 | 38 |
| | Adm FIM cog 11—15 | 24 | 23 | 21 | 20 | 24 | 29 | 29 | 30 | 37 |
| | Adm FIM cog 16—20 | 23 | 19 | 19 | 19 | 19 | 20 | 24 | 21 | 29 |
| | Adm FIM cog ≥21 | 16 | 14 | 14 | 13 | 14 | 15 | 15 | 22 | 19 |
| Anticonvulsant (%) | Overall | 39 | 39 | 39 | 41 | 42 | 43 | 42 | 46 | 48 |
| | Adm FIM cog ≤6 | 37 | 38 | 38 | 42 | 41 | 45 | 43 | 49 | 59 |
| | Adm FIM cog 7—10 | 39 | 39 | 41 | 45 | 52 | 52 | 51 | 52 | 53 |
| | Adm FIM cog 11—15 | 38 | 40 | 41 | 43 | 46 | 48 | 46 | 50 | 52 |
| | Adm FIM cog 16—20 | 41 | 41 | 40 | 41 | 49 | 44 | 40 | 29 | 24 |
| | Adm FIM cog ≥21 | 39 | 34 | 31 | 23 | 12 | 13 | 13 | 22 | 19 |
| Antidepressant (%) | Overall | 56 | 59 | 62 | 65 | 66 | 67 | 66 | 67 | 69 |
| | Adm FIM cog ≤6 | 59 | 65 | 65 | 68 | 71 | 72 | 71 | 63 | 73 |
| | Adm FIM cog 7—10 | 61 | 65 | 69 | 68 | 71 | 72 | 74 | 70 | 62 |
| | Adm FIM cog 11—15 | 58 | 59 | 62 | 67 | 61 | 63 | 65 | 73 | 78 |
| | Adm FIM cog 16—20 | 60 | 63 | 64 | 64 | 68 | 60 | 52 | 63 | 59 |
| | Adm FIM cog ≥21 | 44 | 47 | 47 | 48 | 51 | 54 | 53 | 65 | 63 |
| Antiparkinson (%) | Overall | 16 | 21 | 25 | 29 | 32 | 32 | 32 | 31 | 27 |
| | Adm FIM cog ≤6 | 35 | 41 | 41 | 44 | 44 | 45 | 45 | 42 | 36 |
| | Adm FIM cog 7—10 | 26 | 29 | 32 | 35 | 38 | 42 | 43 | 39 | 32 |
| | Adm FIM cog 11—15 | 15 | 19 | 22 | 25 | 28 | 30 | 25 | 27 | 30 |
| | Adm FIM cog 16—20 | 9 | 14 | 15 | 18 | 18 | 12 | 14 | 13 | 12 |
| | Adm FIM cog ≥21 | 4 | 6 | 7 | 6 | 4 | 3 | 0 | 0 | 0 |
| Antipsychotic (%) | Overall | 20 | 19 | 19 | 20 | 21 | 22 | 23 | 24 | 29 |
| | Adm FIM cog ≤6 | 25 | 24 | 24 | 27 | 27 | 30 | 33 | 35 | 42 |
| | Adm FIM cog 7—10 | 26 | 25 | 23 | 23 | 23 | 25 | 27 | 27 | 29 |
| | Adm FIM cog 11—15 | 24 | 21 | 20 | 21 | 19 | 15 | 17 | 17 | 26 |
| | Adm FIM cog 16—20 | 19 | 19 | 19 | 15 | 16 | 18 | 17 | 8 | 6 |
| | Adm FIM cog ≥21 | 9 | 7 | 8 | 7 | 7 | 7 | 6 | 4 | 6 |

(*continued on next page*)

**Table 3** (*continued*)

| Pharmaceutical Class | FIM Cognitive Score at Admission | Received Week 1 | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Hypnotic (%) | Overall | 21 | 22 | 24 | 26 | 26 | 26 | 25 | 25 | 27 |
| | Adm FIM cog ≤6 | 21 | 24 | 23 | 26 | 26 | 25 | 22 | 25 | 25 |
| | Adm FIM cog 7—10 | 25 | 26 | 29 | 32 | 30 | 34 | 33 | 34 | 38 |
| | Adm FIM cog 11—15 | 23 | 23 | 26 | 31 | 32 | 36 | 35 | 33 | 33 |
| | Adm FIM cog 16—20 | 18 | 18 | 19 | 18 | 18 | 12 | 10 | 0 | 6 |
| | Adm FIM cog ≥21 | 20 | 18 | 18 | 16 | 14 | 14 | 15 | 13 | 19 |
| Narcotic analgesic (%) | Overall | 65 | 60 | 55 | 49 | 49 | 45 | 40 | 42 | 40 |
| | Adm FIM cog ≤6 | 59 | 56 | 52 | 47 | 46 | 45 | 41 | 42 | 41 |
| | Adm FIM cog 7—10 | 63 | 59 | 52 | 47 | 50 | 48 | 44 | 48 | 38 |
| | Adm FIM cog 11—15 | 67 | 60 | 55 | 51 | 50 | 52 | 46 | 47 | 48 |
| | Adm FIM cog 16—20 | 69 | 63 | 58 | 52 | 54 | 36 | 31 | 25 | 29 |
| | Adm FIM cog ≥21 | 66 | 62 | 59 | 48 | 42 | 37 | 30 | 35 | 38 |
| Miscellaneous psychotropic (%) | Overall | 11 | 13 | 15 | 14 | 16 | 18 | 19 | 20 | 18 |
| | Adm FIM cog ≤6 | 6 | 10 | 15 | 19 | 20 | 23 | 27 | 28 | 25 |
| | Adm FIM cog 7—10 | 11 | 13 | 13 | 13 | 16 | 18 | 14 | 20 | 15 |
| | Adm FIM cog 11—15 | 14 | 16 | 18 | 16 | 16 | 15 | 23 | 23 | 19 |
| | Adm FIM cog 16—20 | 15 | 18 | 18 | 14 | 14 | 14 | 12 | 13 | 12 |
| | Adm FIM cog ≥21 | 8 | 8 | 7 | 6 | 7 | 10 | 9 | 4 | 0 |
| Stimulant (%) | Overall | 15 | 21 | 27 | 33 | 38 | 39 | 38 | 35 | 34 |
| | Adm FIM cog ≤6 | 30 | 42 | 46 | 51 | 56 | 57 | 57 | 52 | 49 |
| | Adm FIM cog 7—10 | 25 | 33 | 38 | 43 | 44 | 51 | 49 | 45 | 38 |
| | Adm FIM cog 11—15 | 13 | 18 | 21 | 28 | 33 | 34 | 35 | 30 | 37 |
| | Adm FIM cog 16—20 | 9 | 13 | 13 | 11 | 14 | 6 | 5 | 0 | 0 |
| | Adm FIM cog ≥21 | 4 | 6 | 7 | 7 | 5 | 4 | 4 | 0 | 0 |

Abbreviation: Adm FIM cog, admission FIM cognitive score.

* Ten patients were excluded because of missing admission FIM cognitive scores.

**Table 4** Bivariate associations of patient preinjury and injury characteristics with ever receiving medication during rehabilitation

| Variable | Anxiolytic | | Anticonvulsant | | Antidepressant | | Antiparkinson | | Antipsychotic | | Hypnotic | | Narcotic Analgesic | | Miscellaneous Psychotropic | | Stimulant | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* |
| Age (continuous) (y) | 42±19†; −3‡ | <.001 | 4±22†; 5‡ | <.001 | 44±20†; −3‡ | .008 | 42±20†; −3‡ | .004 | 41±19†; −4‡ | <.001 | 44±20†; −1‡ | .526 | 42±20†; −8‡ | <.001 | 47±20†; 4‡ | .001 | 40±20†; −6‡ | <.001 |
| Age (category) (y) | | <.001 | | <.001 | | <.001 | | .009 | | <.001 | | .018 | | <.001 | | <.001 | | <.001 |
| <30y | 32 | NA | 41 | NA | 67 | NA | 26 | NA | 27 | NA | 28 | NA | 76 | NA | 13 | NA | 33 | NA |
| ≥30–<45y | 40 | NA | 44 | NA | 75 | NA | 30 | NA | 32 | NA | 35 | NA | 82 | NA | 22 | NA | 30 | NA |
| ≥45–<65y | 37 | NA | 50 | NA | 69 | NA | 25 | NA | 26 | NA | 31 | NA | 74 | NA | 21 | NA | 25 | NA |
| ≥65–<75y | 26 | NA | 57 | NA | 59 | NA | 21 | NA | 17 | NA | 31 | NA | 61 | NA | 16 | NA | 20 | NA |
| ≥75–<85y | 19 | NA | 58 | NA | 61 | NA | 16 | NA | 20 | NA | 28 | NA | 53 | NA | 23 | NA | 19 | NA |
| ≥85y | 15 | NA | 44 | NA | 46 | NA | 18 | NA | 6 | NA | 17 | NA | 39 | NA | 17 | NA | 14 | NA |
| Sex | | .959 | | .408 | | .235 | | .082 | | <.001 | | .314 | | .516 | | .077 | | .481 |
| Female | 33 | NA | 48 | NA | 65 | NA | 22 | NA | 20 | NA | 28 | NA | 73 | NA | 16 | NA | 26 | NA |
| Male | 33 | NA | 46 | NA | 68 | NA | 26 | NA | 28 | NA | 31 | NA | 72 | NA | 19 | NA | 28 | NA |
| Race/ethnicity | | <.001 | | .011 | | <.001 | | .014 | | .004 | | <.001 | | .01 | | .003 | | .015 |
| Asian/other/unknown | 19 | NA | 30 | NA | 47 | NA | 18 | NA | 19 | NA | 17 | NA | 58 | NA | 9 | NA | 16 | NA |
| Black | 27 | NA | 49 | NA | 58 | NA | 31 | NA | 23 | NA | 24 | NA | 71 | NA | 14 | NA | 27 | NA |
| White Non-Hispanic | 35 | NA | 47 | NA | 71 | NA | 24 | NA | 27 | NA | 32 | NA | 74 | NA | 20 | NA | 29 | NA |
| White Hispanic | 24 | NA | 47 | NA | 60 | NA | 19 | NA | 15 | NA | 23 | NA | 70 | NA | 15 | NA | 21 | NA |
| History of drug abuse | | .001 | | .957 | | <.001 | | .664 | | <.001 | | .178 | | <.001 | | <.001 | | .51 |
| No | 31 | NA | 47 | NA | 65 | NA | 25 | NA | 23 | NA | 29 | NA | 70 | NA | 16 | NA | 28 | NA |
| Yes | 39 | NA | 47 | NA | 74 | NA | 26 | NA | 35 | NA | 32 | NA | 81 | NA | 27 | NA | 26 | NA |
| History of alcohol abuse | | .06 | | .526 | | <.001 | | .075 | | <.001 | | .03 | | .511 | | <.001 | | .649 |
| No | 31 | NA | 47 | NA | 64 | NA | 26 | NA | 21 | NA | 31 | NA | 72 | NA | 14 | NA | 28 | NA |
| Yes | 35 | NA | 46 | NA | 72 | NA | 23 | NA | 33 | NA | 27 | NA | 73 | NA | 26 | NA | 27 | NA |
| History of psychosis/bipolar disorder/schizophrenia | | .049 | | .05 | | .908 | | .90 | | <.001 | | .556 | | .185 | | .091 | | <.001 |
| No | 32 | NA | 46 | NA | 67 | NA | 25 | NA | 24 | NA | 30 | NA | 72 | NA | 18 | NA | 28 | NA |
| Yes | 43 | NA | 57 | NA | 66 | NA | 24 | NA | 55 | NA | 33 | NA | 79 | NA | 25 | NA | 12 | NA |
| Depression prior to or during acute care | | <.001 | | <.001 | | <.001 | | .441 | | .002 | | <.001 | | <.001 | | .385 | | .11 |
| No | 30 | NA | 44 | NA | 61 | NA | 24 | NA | 24 | NA | 27 | NA | 70 | NA | 17 | NA | 27 | NA |
| Yes | 39 | NA | 53 | NA | 82 | NA | 26 | NA | 30 | NA | 36 | NA | 79 | NA | 19 | NA | 30 | NA |
| Anxiety prior to or during acute care | | <.001 | | <.001 | | <.001 | | .448 | | <.001 | | .064 | | <.001 | | .355 | | .502 |
| No | 29 | NA | 45 | NA | 64 | NA | 25 | NA | 24 | NA | 29 | NA | 69 | NA | 18 | NA | 28 | NA |
| Yes | 50 | NA | 55 | NA | 80 | NA | 23 | NA | 33 | NA | 34 | NA | 86 | NA | 19 | NA | 26 | NA |
| Postresuscitation Glasgow Coma Scale score | | <.001 | | <.001 | | <.001 | | <.001 | | .036 | | .003 | | <.001 | | .238 | | <.001 |
| Intubated/sedated | 41 | NA | 47 | NA | 78 | NA | 31 | NA | 29 | NA | 39 | NA | 79 | NA | 22 | NA | 36 | NA |

(*continued on next page*)

**Table 4** (*continued*)

| Variable | Anxiolytic | | Anticonvulsant | | Antidepressant | | Antiparkinson | | Antipsychotic | | Hypnotic | | Narcotic Analgesic | | Miscellaneous Psychotropic | | Stimulant | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* |
| Mild (13–15) | 29 | NA | 46 | NA | 65 | NA | 14 | NA | 21 | NA | 26 | NA | 76 | NA | 18 | NA | 15 | NA |
| Moderate (9–12) | 27 | NA | 33 | NA | 64 | NA | 17 | NA | 24 | NA | 28 | NA | 76 | NA | 13 | NA | 24 | NA |
| Severe (3–8) | 36 | NA | 40 | NA | 71 | NA | 31 | NA | 29 | NA | 31 | NA | 73 | NA | 17 | NA | 36 | NA |
| Missing | 29 | NA | 57 | NA | 60 | NA | 23 | NA | 23 | NA | 28 | NA | 67 | NA | 18 | NA | 23 | NA |

NOTE. A negative value indicates that the characteristic is less common for those who received the medication class as opposed to those who did not receive the medication class (eg, −3 for age indicates patients who received anxiolytics were on average 3 years younger than those who did not).
Abbreviation: NA, not applicable.
* Values are percentage of patients with that characteristic who received the specified medication class or as otherwise indicated.
† Values are presented as mean ± SD for those patients with that characteristic who received the specified medication class.
‡ The difference between those who received the specified medication class and those who did not receive the specified medication class.

# Results

## Study sample

Our sample of 2130 patients with TBI was 73% men, 74% white, 37% married, and 51% employed at the time of injury. Average age of the sample was 45 years. Cause of injury was most commonly vehicular collisions (56%), followed by falls or flying objects (32%), violence (7%), and sports (2%). Mean RLOS was 27±20 days. The mean Rasch-transformed FIM motor score at admission was 33±19, and the mean Rasch-transformed FIM cognitive score was 37±20. The mean time from injury to rehabilitation admission was 29±34 days. The first article in this supplement[14] further summarizes the demographic and injury characteristics for the sample.

## Patterns of medication administration

### Medication use by admission FIM cognitive categories

Medication use is summarized by admission FIM cognitive score subgroup in tables 2 and 3, based on time-variant factors. For all medication classes except anticonvulsants, use was less frequent among those in the highest FIM cognitive score subgroup than in the lower groups. Conversely, medication use was greater for those with worse cognitive function at the time of rehabilitation admission. Use was higher in the 2 lower FIM cognitive score groups than in the middle and higher functioning subgroups for antiparkinson agents, stimulants, and anxiolytics, whereas antipsychotic and miscellaneous psychotropics had the opposite pattern. In general, higher admission FIM cognitive scores had less antidepressant use. For example, antiparkinson agents were used for 35% and 26% of the patients in the 2 lowest FIM cognitive score subgroups, with frequency decreasing with higher admission cognitive function. Anticonvulsant use was higher for the 2 highest FIM cognitive score groups; however, use did not substantially vary across the 5 subgroups.

The most commonly prescribed agents were narcotic analgesics (72% of the sample), followed in decreasing frequency by antidepressants (67%), anticonvulsants (47%), antianxiety agents (33%), hypnotics (30%), stimulants (28%), antiparkinson agents (25%), antipsychotics (25%), and miscellaneous psychotropics (18%). Expanded detail on the frequency of specific medications at the level of general mechanism within each pharmaceutical class by admission FIM cognitive score category is available in supplemental tables S1 and S2 (available online only at http://www.archives-pmr.org/).

### Anxiolytic agents

The percentage of patients administered anxiolytic medication remained roughly the same from admission to discharge for the overall sample and for all FIM cognitive score subgroups. Only 19% received an anxiolytic during the first 2 days, and 19% received an anxiolytic during the last 2 days, with 33% receiving this class at some point during the stay. The primary anxiolytic prescribed was benzodiazepine, with 29% of patients receiving it at some point during the rehabilitation stay: approximately half of individuals received it on a regular basis, and half received it on a PRN basis. Lorazepam was the most common benzodiazepine prescribed, accounting for 68% of the benzodiazepine-based anxiolytics administered, followed by clonazepam (12%), and alprazolam (10%). H1 receptor antagonists (ie, hydroxyzine) were

**Table 5** Bivariate associations of rehabilitation characteristics with ever receiving medication during rehabilitation

| | Anxiolytic | | Anticonvulsant | | Antidepressant | | Antiparkinson | |
|---|---|---|---|---|---|---|---|---|
| Variable | %* | *P* | %* | *P* | %* | *P* | %* | *P* |
| Seizure any time up to rehabilitation discharge | | .023 | | <.001 | | .153 | | .621 |
| No seizure | 32 | NA | 41 | NA | 68 | NA | 25 | NA |
| Yes, ≥1 seizure | 38 | NA | 80 | NA | 63 | NA | 26 | NA |
| Days from injury to rehabilitation admission | 35±42†; 8‡ | <.001 | 28±32†; −3‡ | .036 | 31±37†; 7‡ | <.001 | 37±40†; 10‡ | <.001 |
| Admission FIM cognitive category | | <.001 | | .031 | | <.001 | | <.001 |
| Score ≤6 | 48 | NA | 50 | NA | 77 | NA | 53 | NA |
| Score 7–10 | 44 | NA | 52 | NA | 76 | NA | 40 | NA |
| Score 11–15 | 31 | NA | 46 | NA | 66 | NA | 21 | NA |
| Score 16–20 | 28 | NA | 46 | NA | 69 | NA | 15 | NA |
| Score ≥21 | 20 | NA | 41 | NA | 53 | NA | 6 | NA |
| Admission FIM motor category | | <.001 | | .167 | | <.001 | | <.001 |
| Score <22.05 | 44 | NA | 50 | NA | 77 | NA | 43 | NA |
| Score 22.05–28.75 | 30 | NA | 46 | NA | 58 | NA | 21 | NA |
| Score 28.75–40.65 | 31 | NA | 46 | NA | 70 | NA | 16 | NA |
| Score 40.65–44.25 | 23 | NA | 46 | NA | 67 | NA | 12 | NA |
| Score 44.25–53.36 | 24 | NA | 46 | NA | 66 | NA | 14 | NA |
| Score >53.36 | 21 | NA | 41 | NA | 51 | NA | 9 | NA |
| % of days with <5h sleep | 36±23†; 8‡ | <.001 | 33±23†; 3‡ | <.001 | 32±22†; 2‡ | .079 | 34±22†; 5‡ | <.001 |
| Average therapy level of effort | 4±1†; −0.4‡ | <.001 | 4±1†; −0.2‡ | <.001 | 4±1†; −0.3‡ | <.001 | 4±1†; −0.8‡ | <.001 |
| Maximum CSI brain injury component | 59±25†; 16‡ | <.001 | 50±25†; 4‡ | <.001 | 52±25†; 12‡ | <.001 | 67±23†; 24‡ | <.001 |
| Maximum CSI nonbrain injury component | 30±24†; 7‡ | <.001 | 26±22†; 3‡ | <.001 | 27±21†; 6‡ | <.001 | 30±23†; 6‡ | <.001 |
| PTA duration (d) | 49±54†; 18‡ | <.001 | 40±46†; 4‡ | .045 | 42±47†; 14‡ | <.001 | 61±54†; 32‡ | <.001 |
| Time of PTA clearing | | <.001 | | .151 | | <.001 | | <.001 |
| Cleared PTA prior to rehabilitation admission | 26 | NA | 47 | NA | 64 | NA | 11 | NA |
| Cleared PTA on rehabilitation admission day | 14 | NA | 40 | NA | 44 | NA | 12 | NA |
| Cleared PTA after rehabilitation admission day | 39 | NA | 50 | NA | 72 | NA | 36 | NA |
| % of days with pain score ≥7 | 20±26†; 4‡ | <.001 | 20±27†; 5‡ | <.001 | 19±26†; 7‡ | <.001 | 12±20†; −7‡ | <.001 |
| % of rehabilitation stay agitated | 16±25†; 10‡ | <.001 | 11±22†; 5‡ | <.001 | 11±21†; 5‡ | <.001 | 13±22†; 5‡ | <.001 |

NOTE. A negative value indicates that the characteristic is less common for those who received the medication class as opposed to those who did not receive the medication class (eg, 8 for days injury to rehabilitation admission indicates that the patient who received anxiolytics had on average 8 days longer from injury to rehabilitation admission than those who did not).

Abbreviation: NA, not applicable.

* Values are percentage of patients with that characteristic who received the specified medication class or as otherwise indicated.

† Values are mean ± SD for those patients with that characteristic who received the specified medication class.

‡ The difference between those who received the specified medication class and those who did not receive the specified medication class.

rarely used and were prescribed PRN more often than scheduled. Of the entire sample, 7% of patients received buspirone, which was predominately prescribed on a scheduled basis, with usage increasing over the RLOS.

### Anticonvulsant agents

Nearly half (47%) of patients received an anticonvulsant at some point during their rehabilitation stay, with 35% receiving 1 during the first 2 days, 39% receiving 1 during the last 2

| Antipsychotic | | Hypnotic | | Narcotic Analgesic | | Miscellaneous Psychotropic | | Stimulant | |
|---|---|---|---|---|---|---|---|---|---|
| %* | *P* | %* | *P* | %* | *P* | %* | *P* | %* | *P* |
| | .208 | | .463 | | <.001 | | .011 | | .785 |
| 26 | NA | 30 | NA | 74 | NA | 17 | NA | 28 | NA |
| 23 | NA | 28 | NA | 64 | NA | 23 | NA | 28 | NA |
| 29±32†; 0‡ | .998 | 31±30†; 2‡ | .159 | 28±33†; −6‡ | .001 | 29±33†; −0‡ | .937 | 37±43†; 10‡ | <.001 |
| | <.001 | | <.001 | | .204 | | <.001 | | <.001 |
| 38 | NA | 36 | NA | 71 | NA | 24 | NA | 57 | NA |
| 34 | NA | 37 | NA | 74 | NA | 19 | NA | 44 | NA |
| 28 | NA | 31 | NA | 73 | NA | 21 | NA | 25 | NA |
| 22 | NA | 25 | NA | 75 | NA | 19 | NA | 15 | NA |
| 10 | NA | 24 | NA | 69 | NA | 10 | NA | 8 | NA |
| | <.001 | | <.001 | | <.001 | | .604 | | <.001 |
| 29 | NA | 37 | NA | 77 | NA | 19 | NA | 45 | NA |
| 30 | NA | 28 | NA | 72 | NA | 16 | NA | 27 | NA |
| 25 | NA | 27 | NA | 77 | NA | 19 | NA | 18 | NA |
| 23 | NA | 26 | NA | 79 | NA | 14 | NA | 14 | NA |
| 26 | NA | 27 | NA | 68 | NA | 17 | NA | 16 | NA |
| 17 | NA | 23 | NA | 59 | NA | 17 | NA | 14 | NA |
| 33±22†; 3‡ | .005 | 36±23†; 8‡ | <.001 | 33±23†; 7‡ | <.001 | 31±23†; 0‡ | .936 | 31±20†; −0‡ | .942 |
| 4±1†; −0.4‡ | <.001 | 4±1†; −0.2‡ | <.001 | 4±1†; 0.0‡ | .618 | 4±1†; −0.3‡ | <.001 | 4±1†; −0.6‡ | <.001 |
| 58±22†; 13‡ | <.001 | 55±25†; 10‡ | <.001 | 50±25†; 5‡ | <.001 | 55±24†; 8‡ | <.001 | 66±23†; 25‡ | <.001 |
| 30±23†; 7‡ | <.001 | 30±23†; 7‡ | <.001 | 27±22†; 9‡ | <.001 | 24±19†; −1‡ | .578 | 28±21†; 5‡ | <.001 |
| 45±47†; 10‡ | <.001 | 44±45†; 9‡ | <.001 | 37±42†; −2‡ | .324 | 43±44†; 7‡ | .006 | 60±54†; 31‡ | <.001 |
| | <.001 | | <.001 | | .007 | | <.001 | | <.001 |
| 17 | NA | 28 | NA | 78 | NA | 14 | NA | 12 | NA |
| 9 | NA | 9 | NA | 88 | NA | 14 | NA | 9 | NA |
| 32 | NA | 33 | NA | 73 | NA | 21 | NA | 40 | NA |
| 18±24†; 1‡ | .528 | 19±26†; 3‡ | .007 | 23±27†; 20† | <.001 | 19±27†; 2‡ | .117 | 11±18†; −8‡ | <.001 |
| 20±27†; 15‡ | <.001 | 13±24†; 6‡ | <.001 | 9±20†; 2† | .04 | 14±24†; 6‡ | <.001 | 13±23†; 6‡ | <.001 |

days, and 28% receiving 1 during both intervals. The most commonly used anticonvulsants were the calcium channel and sodium channel antagonists. The most common calcium channel antagonist used was levetiracetam (61% of agents in this class administered to 21% of the sample); the most common sodium channel antagonists used were valproic acid (39% of agents in this class), phenytoin (37%), and carbamazepine (9%).

### Antidepressant agents

Two thirds of the patients (67%) received an antidepressant at some point during their rehabilitation stay: 44% during the first 2 days, 55% the last 2 days, and 37% during both intervals. The most commonly used antidepressants were serotonin antagonist and reuptake inhibitors (SARIs) (ie, trazodone) and selective serotonin reuptake inhibitors (ie, citalopram, escitalopram, fluoxetine, paroxetine, sertraline); only a minority of patients received tricyclic antidepressants (ie, desipramine, nortriptyline, amitriptyline, doxepin), norepinephrine-dopamine reuptake inhibitors (ie, bupropion), noradrenergic and specific serotonergic antidepressants (ie, mirtazapine), and serotonin and norepinephrine reuptake inhibitors (ie, duloxetine, venlafaxine, and milnacipran). Antidepressants were generally prescribed as scheduled with only occasional PRN use, with the exception of SARI (ie, trazodone), which was used in both manners, consistent the common practice of prescribing this agent for insomnia.

### Antiparkinson agents

Antiparkinson agents were administered to only 25% of the patients at some point during rehabilitation, with use substantially increasing over the stay, from 11% receiving this class of medication during the first 2 days to 20% receiving this class during the last 2 days. The most commonly used antiparkinson medication was an N-methyl-D-aspartate antagonist (ie, amantadine), administered to 17% of the sample, followed by a dopamine agonist (ie, bromocriptine, pramipexole, ropinirole). These agents were generally administered on a scheduled basis with rare PRN use. Bromocriptine accounted for 95% of the dopamine agonists administered.

### Stimulant agents

Stimulants were administered to only 28% of the sample. Similar to the antiparkinson and miscellaneous therapeutic agents, stimulants were predominately started after admission. Use of stimulants increased over the course of the stay, and these agents were commonly used among those with long RLOSs. Patterns of administration appear consistent within the various agents contained in the stimulant class. The most commonly used were the norepinephrine-dopamine-5HT agonists (ie, agents containing amphetamine, dextroamphetamine, or methylphenidate), which were used by 23% of the sample. Less commonly used were armodafinil/modafinil and the norepinephrine agonist atomoxetine. The stimulant agents were generally used on a scheduled basis.

### Antipsychotic agents

Antipsychotic agents were received by a quarter of the sample at some point during their stay. The overall percentage of use did not increase during the stay, with 16% receiving it in the first 2 days, 15% receiving it in the last 2 days, and 10% receiving it during both intervals. Second-generation antipsychotics were administered more frequently (24% of the sample) than first-generation ones (3%). Second-generation medications were most commonly received as scheduled but were also used PRN. On the other hand, first-generation antipsychotics were more often administered PRN than scheduled. Those with longer RLOSs had slightly higher usage. Of the second-generation antipsychotics administered, quetiapine accounted for 48%, followed by risperidone (19%), olanzapine (15%), and ziprasidone (14%).

### Hypnotic agents

Hypnotic agents were administered to 30% of the sample. Use increased slightly from admission to later in the stay and was particularly common for those with longer RLOSs. Most commonly prescribed in this class were nonbenzodiazepine gamma-aminobutyric acid-A agonists (ie, zolpidem [88% of the class], eszopiclone [11%], zaleplon [<1%]), followed by occasional (5%) use of benzodiazepine gamma-aminobutyric acid-A agonists (ie, temazepam [62% of the class], midazolam [38% of the class]), and 3% use of other hypnotics (ie, chloral hydrate, propofol, phenobarbital). Melatonin agonists were rarely used. In general, hypnotics were slightly more likely to be used PRN than scheduled.

### Miscellaneous psychotropic agents

Miscellaneous psychotropics were used relatively less often than other agents, with 18% of patients receiving 1 of these agents at some point during their rehabilitation stay. They were most commonly initiated later in the stay and more frequently administered to those with longer RLOSs. The most commonly prescribed in this class were acetylcholinesterase inhibitors (AChEIs) (ie, donepezil, physostigmine, rivastigmine) at 9% and others (ie, glatiramer acetate, interferon beta-1a, nicotine, varenicline) at 9%. The AChEIs were generally prescribed after rehabilitation admission and later in the stay. Use was greatest in the later weeks of the rehabilitation stay and for those with longer RLOSs. On the other hand, administration of the other psychotherapeutics was greatest during the first 2 days of rehabilitation, with decreased use over the remaining stay. For those with longer RLOSs, these agents were used less over time. These findings are largely accounted for by the prescription of nicotine or nicotine patch, which accounted for 98% of the use in the other category. This class of medications was most commonly administered as scheduled with occasional PRN use. The AChEIs were used PRN for 17% of the patients receiving this agent.

### Narcotic analgesics

Most patients received narcotics during their rehabilitation stay (72% overall), with a high use across FIM categories, even among those with lower levels of function. Most of the use occurred at admission (55% of the sample during the first 2 days of rehabilitation), with decreased use occurring over the rehabilitation stay: 45% of the sample received narcotic analgesics during the last 2 days of rehabilitation. Narcotics were consumed for an average of 16 days, accounting for a mean 65% of the RLOS administered. Narcotics were received as both scheduled and PRN. PRN administration was used as commonly in the lower functioning group who are expected to have impaired communication as in the higher functioning groups. Scheduled use occurred across functional groups with less scheduled narcotic administration in the highest functioning group.

## Relation of patient factors and medication administration

Table 4 shows the relation between receiving a medication from a psychotropic pharmaceutical class at any time during rehabilitation and preinjury characteristics and injury-related variables. Age was highly associated with receiving most medications, with the exception being hypnotics. In general, younger patients were more likely to receive anxiolytics, antidepressants, antiparkinsons, stimulants, antipsychotics, and narcotic analgesics. In contrast, older patients were more likely to receive

anticonvulsants and miscellaneous psychotropics. Men were more likely to receive antipsychotics. History of psychosis, bipolar disorder, or schizophrenia was also associated with being more likely to receive an antipsychotic, but it was unrelated to receiving other classes of medications. Anxiolytics, antidepressants, and hypnotics were less likely to be used in minority populations. Anxiolytics, anticonvulsants, antidepressants, and narcotic analgesics were more likely to be used when there was a history of depression or anxiety (premorbid history or during acute care). Antidepressants, antipsychotics, and psychotropics were more likely to be used when a patient had a prior history of substance abuse.

In contrast with table 4, table 5 shows the relation between having ever been administered a medication and patient characteristics during the rehabilitation stay. Multiple indices of more severe impairment (percentage of stay agitated, effort given in therapies, severity of brain impairment, severity of nonbrain comorbidities, length of PTA) were related to increased drug administration in nearly all categories. Other indices indicative of greater difficulties during rehabilitation (ie, percentage of days in pain, percentage of days with <5h of sleep) were related to increased medication administration, with the exceptions of antipsychotics and psychotropics. Having seizures during rehabilitation increased the likelihood of administration of anticonvulsants and narcotic analgesics.

### Psychotropic medication exposure summary and concurrent use

Table 6 depicts the percentage of patients receiving specific quantities of psychotropic medications during rehabilitation, overall, and by admission cognitive category. Only 5% of the patients were never administered psychotropic medications during their rehabilitation stay, whereas 8.5% were prescribed only 1 of the psychotropic medications; 31.8% were prescribed ≥6 of these agents at some point during their stay. These results could occur if all 6 were prescribed simultaneously or sequentially (1 after the other) while the physician was searching for an effective drug. It is more likely that some were given at the same time, with some dropping off and others being added. During the first 2 days of rehabilitation, 5.5% of patients were on at least 6 psychotropic medications, whereas 13.5% were on at least 6 of these medications during the last 2 rehabilitation days. In general, those in the lower admission FIM cognitive score categories received a greater number of psychotropic medications (3−8 agents) than those in the higher FIM cognitive score categories, in which most received 0 to 5 agents.

### Medication administration across sites

Medication administration patterns varied greatly across treatment sites as summarized in table 7. Sites with high antipsychotic use had lower use of anxiolytics and vice versa. Sites with high antiparkinson administration had less antipsychotic use and vice versa. For anticonvulsant use, most sites were similar except 1 site where 80% of patients received an anticonvulsant agent during their rehabilitation stay. With a range of 7% to 31%, miscellaneous psychotropic agents were used relatively infrequently at some sites. Antidepressant use was uncommon at 1 site (27%), with use ranging from 46% to 91% across the other sites. The site with the highest use of antidepressants had a practice pattern of using the antidepressants SARIs and tertiary amine tricyclic antidepressants as their first-line treatment of insomnia. Across sites, antiparkinson agent use ranged from 1% to 57% and stimulants use ranged from 5% to 50%.

## Discussion

This large sample, multicenter study documents the extent to which psychotropic medications are administered to treat patients with TBI during inpatient rehabilitation. In 9 broad categories of medications, the percentage of overall use varied from 18% to 72%, with a mean of 42% (see table 2, % ever received). Of the participants, 31.8% were exposed to at least 6 of the psychotropic agents studied during rehabilitation (see table 6). These results suggest a strong culture of intervention,[20] with the prevalent use of unproven medications to advance recovery in this group of facilities that specialize in brain injury management; an urgent need to control patient behavior; and/or a strong desire to stimulate recovery. We found considerable variation across sites. Marked variation in clinical practice is likely a reflection of the relative lack of high-quality research available in neuropharmacology post-TBI. With the absence of solid data, clinicians may base their treatment decisions on information gleaned from accepted treatments for other impairment groups with similar problems to treat issues such as agitation, headache, pain, insomnia, and sleep disorder. In the absence of better evidence, the prescriber is often reliant on their subjective clinical impressions, expert opinion, and a multitude of case studies and open-label case series reinforced by and overlying natural recovery.

In this study, univariate analyses indicated potential differences related to age and race in the percentage of patients prescribed varying classes of medications. The extent to which younger patients may be more likely to be administered anxiolytics, antidepressants, antiparkinsons/stimulants, antipsychotics, and narcotic analgesics requires further analysis that controls for injury severity and secondary conditions. Further testing for nonlinear relations between age and medication administration (ie, both very young and very old patients being less likely to be prescribed medications) is also warranted.[21] Anxiolytics, antidepressants, antipsychotics, hypnotics, and antiparkinson agents were less likely to be used with ethnic minorities, particularly those of Asian and Hispanic descent. Given the relatively small number of Asian and Hispanic patients in this sample, further investigation is warranted to evaluate the extent that injury severity and secondary conditions versus unmeasured factors (eg, differential cultural preferences, site differences in ethnicity and prescribing preferences) are related to medication use.

This study did not capture information about the primary symptom(s) that physicians targeted for each medication prescribed. Tables 4 and 5 indirectly provide insight into the potential variability in symptoms associated with the pharmaceutical classes of medication administered. For example, 29% of those who received anxiolytics did not have anxiety mentioned in their medical record (as having been present premorbidly, during acute care, or at the time of rehabilitation admission), suggesting that many may be treated with this class of medication for other reasons (eg, agitation, insomnia). Similarly, 61% of those who received antidepressants did not have mention of depression present premorbidly or during acute care, suggesting that pain, sleep disorders, and/or behavior are being treated by commonly

**Table 6** Percentage of patients who received psychoactive medications during rehabilitation by number received and admission cognitive functional level

| No. of Psychoactive Medications Received | Overall | | | Adm FIM Cog ≤6 | | | Adm FIM Cog 7–10 | | | Adm FIM Cog 11–15 | | | Adm FIM Cog 16–20 | | | Adm FIM Cog ≥21 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % Ever Received | % Received First 2d | % Received Last 2d | % Ever Received | % Received First 2d | % Received Last 2d | % Ever Received | % Received First 2d | % Received Last 2d | % Ever Received | % Received First 2d | % Received Last 2d | % Ever Received | % Received First 2d | % Received Last 2d | % Ever Received | % Received First 2d | % Received Last 2d |
| 0 | 5.0 | 13.0 | 12.7 | 2.4 | 13.9 | 7.7 | 2.4 | 11.8 | 9.4 | 4.4 | 11.5 | 14.1 | 4.2 | 9.6 | 10.8 | 10.1 | 17.3 | 18.7 |
| 1 | 8.5 | 21.9 | 17.3 | 3.2 | 15.6 | 10.3 | 4.5 | 20.6 | 10.7 | 7.5 | 23.0 | 15.2 | 8.6 | 22.1 | 19.9 | 16.3 | 25.6 | 27.4 |
| 2 | 12.6 | 23.4 | 17.4 | 5.9 | 24.2 | 15.9 | 7.0 | 21.1 | 14.7 | 10.7 | 21.6 | 16.6 | 15.7 | 25.2 | 19.1 | 20.4 | 25.0 | 19.8 |
| 3 | 14.6 | 17.5 | 17.0 | 9.7 | 18.0 | 16.2 | 11.2 | 18.2 | 16.8 | 17.4 | 19.4 | 19.0 | 16.2 | 18.6 | 17.6 | 16.3 | 13.9 | 15.5 |
| 4 | 14.3 | 12.0 | 13.9 | 10.9 | 14.2 | 16.2 | 12.6 | 11.0 | 17.4 | 15.8 | 14.5 | 14.1 | 17.2 | 10.5 | 14.2 | 14.3 | 10.1 | 9.1 |
| 5 | 12.9 | 6.6 | 8.4 | 14.7 | 6.2 | 10.6 | 13.9 | 9.6 | 10.4 | 13.5 | 6.1 | 8.5 | 14.2 | 7.4 | 8.1 | 9.5 | 4.4 | 5.2 |
| 6 | 10.4 | 3.5 | 6.0 | 11.2 | 5.0 | 11.2 | 15.5 | 5.3 | 7.0 | 13.1 | 1.8 | 7.1 | 8.8 | 3.9 | 3.4 | 4.4 | 2.4 | 2.8 |
| 7 | 7.3 | 1.4 | 3.8 | 12.4 | 1.8 | 6.8 | 11.0 | 1.3 | 7.2 | 5.5 | 1.4 | 2.2 | 4.7 | 1.7 | 3.7 | 5.0 | 1.0 | 0.8 |
| 8 | 4.9 | 0.5 | 1.5 | 8.8 | 0.9 | 2.9 | 7.2 | 0.8 | 2.7 | 4.4 | 0.2 | 0.8 | 3.9 | 0.5 | 1.0 | 2.0 | 0.4 | 0.8 |
| 9 | 3.5 | 0.1 | 1.1 | 6.5 | 0.3 | 1.2 | 4.5 | 0.3 | 1.6 | 2.2 | 0.0 | 1.6 | 3.7 | 0.2 | 1.0 | 1.6 | 0.0 | 0.0 |
| 10 | 2.2 | 0.0 | 0.3 | 4.1 | 0.0 | 0.0 | 4.5 | 0.0 | 1.1 | 1.8 | 0.2 | 0.4 | 1.2 | 0.0 | 0.2 | 0.2 | 0.0 | 0.0 |
| >10 | 3.5 | 0.0 | 0.4 | 10.0 | 0.0 | 0.9 | 5.7 | 0.0 | 1.0 | 3.6 | 0.2 | 0.4 | 1.6 | 0.2 | 0.9 | 0.0 | 0.0 | 0.0 |

Abbreviation: Adm FIM Cog, admission FIM cognitive subscale.

**Table 7** Percentage that received medication classification by treatment site

| Variable | Anxiolytic | Anticonvulsant | Antidepressant | Antiparkinson | Antipsychotic | Hypnotic | Narcotic Analgesic | Miscellaneous Psychotropic | Stimulant |
|---|---|---|---|---|---|---|---|---|---|
| | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* | % Patients Received* |
| Site 1 | 39 | 42 | 52 | 10 | 14 | 23 | 77 | 11 | 12 |
| Site 2 | 50† | 42 | 91† | 57† | 18 | 49† | 87 | 23 | 50† |
| Site 3 | 17‡ | 44 | 50 | 4 | 62† | 13‡ | 79 | 9 | 40 |
| Site 4 | 20 | 46 | 64 | 16 | 13‡ | 18 | 78 | 7‡ | 5‡ |
| Site 5 | 21 | 60 | 64 | 25 | 24 | 21 | 58 | 37† | 40 |
| Site 6 | 20 | 51 | 46 | 11 | 27 | 13‡ | 48 | 8 | 28 |
| Site 7 | 33 | 52 | 89 | 25 | 35 | 29 | 90† | 31 | 25 |
| Site 8 | 27 | 80† | 27‡ | 46 | 23 | 31 | 49 | 21 | 6 |
| Site 9 | 38 | 47 | 76 | 33 | 28 | 44 | 77 | 15 | 35 |
| Site 10 | 22 | 22‡ | 48 | 1‡ | 15 | 15 | 33‡ | 12 | 5‡ |
| Average | 29 | 49 | 61 | 23 | 26 | 26 | 68 | 17 | 25 |

* All $P$ values were <.001 for differences across sites.
† Highest percentage for medication class.
‡ Lowest percentage for medication class.

prescribed medications that were classified as antidepressants. For example, the SARI trazodone is often used in this population for sleep induction. Similar findings were observed for antipsychotics (24% lacked mention of premorbid history of psychosis, bipolar disorder, or schizophrenia). Of those administered anticonvulsants, 41% did not have a seizure during acute care or rehabilitation, indicating use for seizure prophylaxis or other reasons (eg, behavior control, pain management). The broad range of medication applications highlights the importance of patient education and communication with cotreating physicians regarding the targeted use of medications prescribed at the time of discharge from rehabilitation and after.

Our univariate analyses found statistically significant center effects across pharmaceutical classes. Given the wide variability between centers with regard to age, time from injury to rehabilitation admission, injury etiology and severity, and levels of functional impairment,[22] further analyses are required to determine the extent that center effects exist independent of other confounds. With the limited literature on neuropharmacology effectiveness post-TBI to guide treatment decisions, practice variation at least between physicians would not be surprising.[23,24]

Antiparkinson and stimulant administration were low in comparison with our expectations and in comparison with other psychotropic medications (narcotic analgesics, antidepressants, anticonvulsants, anxiolytics, hypnotics). Antiparkinson agents were administered to 25% of patients at some point during rehabilitation (most commonly amantadine and bromocriptine). In clinical practice, these medications are often used in the treatment of several rehabilitation-relevant issues, including poor arousal, agitation, disinhibition, lack of initiation, akinetic mutism, and cognitive impairment. Similarly, stimulant administration (28% of the sample received) was surprisingly low given that symptoms of inattention, lack of initiation, poor arousal, and slow processing speed are cardinal features of moderate and severe TBI. Stimulants were administered predominately to those with lower admission FIM cognitive scores. The most commonly used stimulants were methylphenidate, modafanil, and atomoxetine. Considering the greater use of other classes (eg, antidepressants, anticonvulsants, anxiolytics, hypnotics), perhaps antiparkinson and stimulant agents could have a greater role in the management of patients with TBI (eg, the agitated, confused, difficult to manage, or slow to recover patient)[25-30] than is currently being used by some physicians. In studies of subacute TBI, patients receiving methylphenidates have shown short-term improvements in attention, concentration, motor memory, cognitive processing speed, and overall function.[26,27] Scientific evidence suggests amantadine may help minimize the impact of many deficits commonly found after TBI, particularly disordered consciousness, cognitive impairments, and behavioral dysregulation.[3,29-31]

Conversely, prescription of narcotics was surprisingly high, despite the risk of their cognitive sedating properties. Narcotic use is very high across all functional cognitive levels, with nearly 75% of all patients receiving these medications at least once during their stay. Although narcotics were overwhelmingly prescribed on a PRN basis, the median percentage of days that patients were administered these medications suggests that in practice they were fairly regularly used. Applying these findings clinically, the clinician is advised to use caution with administering pain medication and consider incorporation of objective measures of function and pain into the assessment and ongoing administration.

Antipsychotic agents were received by 25% of the sample at some point during their stay. It is common for practitioners to use this class of medication to assist with controlling agitation post-TBI. This particular use is somewhat controversial because the blocking of dopamine is not always considered to be productive in terms of recovery.[1,4] However, second-generation antipsychotics have less D2 dopamine receptor effects and are thought to be preferable over first-generation agents; however, they still have a considerable side-effect profile. Second-generation antipsychotics have been proposed by some in the field as preferred treatment for agitation and psychosis as a result of TBI.[32,33] Quetiapine accounted for 48% of the second-generation antipsychotics administered, followed by risperdone (19%), olanzapine (15%), and ziprasidone (14%).

## Future research directions

The use of this multicenter, longitudinal data to evaluate the effectiveness of medication treatments in real-world clinical settings offers both opportunities and challenges. Findings from this initial investigation of medication administration patterns during TBI inpatient rehabilitation provide valuable data that can inform the research design of future medication comparative effectiveness studies. Of the patients in our study, 90% were administered $\geq$2 psychotropic medications during their stay, with 60% administered between 3 and 7. Because of the administration of multiple medications at the same time or within the short time frame of rehabilitation, future research requires that study designs carefully evaluate the effects of psychotropic medications alone and in combination on the primary outcomes of interest. Future research will also need to take into account dosing levels and duration of treatment, while controlling for participant-specific effects. Mixed-effects quantile stratification propensity adjustment strategies for longitudinal analyses may be suited for such treatment effectiveness analyses.[34,35] Based on our findings, participant effects that should be considered for stratified propensity adjustment for each primary outcome include age, timing of administration, history of axis I mental health disorders, severity of cognitive impairment, and pain. The potential confounding effects of center and race should be further evaluated to determine whether these are true effects or are encapsulated within the covariates already listed for potential stratification adjustment. Evaluation and, where necessary, adjustment of individual covariates for nonlinear relations and outlier effects are essential given the frequent observance of large SDs.

## Study limitations

The findings of this study represent the patterns of administration at highly specialized brain injury rehabilitation centers and may not represent the patterns of use at all rehabilitation units. In particular, this study may be unique in regard to the medical complexity and neurologic functional level of the patients, training and experience of the clinicians, academic environment, resources of the facilities, and demographics of the study sample (primarily white). The acute care hospital medical records were not consistently available; therefore, we did not include medications used during acute care. The study focused on key agents commonly used to improve arousal, improve behavior, improve function, and control central nervous system issues associated with TBI. The study was limited

to 9 medications categories. There are several psychotropic medications that were not examined here but were administered (eg, alpha agonist and beta-blocking antihypertensive agents, metoclopramide, proton pump inhibitors, a host of agents with anticholinergic effects).

The targeted goals for medication prescription are not known in this study. Medications designed and approved for 1 use are commonly used for other purposes. For instance, antidepressants may be useful for correction of sleep disorders, pain, and anxiety and depression. Anxiolytics may be used for sleep and behavior modification and anxiety. Anticonvulsants are commonly used for neuropathic pain and mood stabilization and seizure prevention or management. Antipsychotics may be administered for insomnia, anxiety, psychosis, and agitation. The present study reveals the type of psychotropic agents used but not the purpose. Data about severity of injury, duration of PTA, agitation, pain, seizures, sleep, and cognition were assessed for association with administration of these agents and thereby provide some information on use. However, caution should be used in presuming the use of the medications in this study.

## Conclusions

Many psychotropic medications are used during inpatient rehabilitation. A wide variety of applications are perceived for each class of psychotropic medications and individual agents within classes. Knowledge of prescribing patterns may inform further research (eg, comparative effectiveness studies). In general, lower admission FIM cognitive score groups were administered more of the medications under investigation compared with those with higher cognitive function at admission. Considerable site variation existed regarding medications administered.

## Keywords

Amantadine; Antidepressive agents; Antipsychotic agents; Brain injuries; Central nervous system stimulants; Drug therapy; Medication therapy management; Patient care; Physician's practice patterns; Polypharmacy; Rehabilitation

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**Supplemental Table S1** Expanded psychoactive medications data administered by pharmaceutical class and level of admission cognitive function

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anxiolytics | Overall | 2130 | 33 | 19 | 19 | 11 | 23 | 17 | 12 | 56 | 58 | 37 | 53 | 10 |
| | Adm FIM cog ≤6 | 339 | 48 | 24 | 26 | 14 | 31 | 21 | 18 | 50 | 50 | 40 | 45 | 14 |
| | Adm FIM cog 7–10 | 374 | 44 | 23 | 26 | 12 | 32 | 19 | 14 | 53 | 52 | 37 | 55 | 7 |
| | Adm FIM cog 11–15 | 495 | 31 | 18 | 18 | 11 | 22 | 17 | 13 | 60 | 67 | 36 | 57 | 7 |
| | Adm FIM cog 16–20 | 408 | 28 | 20 | 17 | 13 | 20 | 13 | 9 | 62 | 73 | 33 | 56 | 11 |
| | Adm FIM cog ≥21 | 504 | 20 | 13 | 12 | 7 | 14 | 12 | 10 | 60 | 65 | 39 | 50 | 11 |
| Anxiolytics: GABA-A | Overall | 2130 | 29 | 17 | 15 | 8 | 18 | 16 | 10 | 50 | 44 | 44 | 47 | 9 |
| | Adm FIM cog ≤6 | 339 | 46 | 22 | 21 | 11 | 27 | 18 | 10 | 43 | 27 | 44 | 42 | 14 |
| | Adm FIM cog 7–10 | 374 | 39 | 22 | 20 | 9 | 26 | 18 | 13 | 50 | 47 | 44 | 49 | 7 |
| | Adm FIM cog 11–15 | 495 | 26 | 15 | 14 | 8 | 17 | 16 | 12 | 55 | 54 | 43 | 51 | 6 |
| | Adm FIM cog 16–20 | 408 | 24 | 17 | 12 | 9 | 15 | 11 | 8 | 52 | 43 | 43 | 48 | 9 |
| | Adm FIM cog ≥21 | 504 | 17 | 12 | 9 | 6 | 11 | 11 | 7 | 55 | 51 | 46 | 45 | 9 |
| Anxiolytics: H1 | Overall | 2130 | >0 | >0 | >0 | >0 | >0 | 9 | 5 | 36 | 27 | 59 | 27 | 14 |
| | Adm FIM cog ≤6 | 339 | >0 | >0 | >0 | >0 | 0 | 12 | 15 | 51 | 38 | 67 | 33 | 0 |
| | Adm FIM cog 7–10 | 374 | 1 | >0 | >0 | 0 | 0 | 16 | 3 | 26 | 7 | 60 | 40 | 0 |
| | Adm FIM cog 11–15 | 495 | >0 | 0 | 0 | 0 | 0 | 2 | 2 | 8 | 5 | 100 | 0 | 0 |
| | Adm FIM cog 16–20 | 408 | >0 | >0 | >0 | >0 | 0 | 9 | 9 | 60 | 50 | 33 | 4 | 62 |
| | Adm FIM cog ≥21 | 504 | 1 | >0 | >0 | >0 | 0 | 7 | 6 | 42 | 32 | 40 | 44 | 17 |
| Anxiolytics: other | Overall | 2130 | 7 | 3 | 6 | 2 | 6 | 21 | 17 | 68 | 77 | 2 | 85 | 13 |
| | Adm FIM cog ≤6 | 339 | 9 | 3 | 6 | 2 | 9 | 26 | 25 | 63 | 68 | 3 | 78 | 19 |
| | Adm FIM cog 7–10 | 374 | 10 | 3 | 8 | 2 | 9 | 22 | 17 | 62 | 63 | 3 | 87 | 11 |
| | Adm FIM cog 11–15 | 495 | 8 | 4 | 6 | 3 | 7 | 22 | 15 | 71 | 82 | 0 | 92 | 8 |
| | Adm FIM cog 16–20 | 408 | 8 | 4 | 7 | 3 | 6 | 15 | 13 | 72 | 88 | 3 | 84 | 13 |
| | Adm FIM cog ≥21 | 504 | 3 | 1 | 2 | >0 | 3 | 20 | 17 | 85 | 84 | 0 | 85 | 15 |
| Anticonvulsants | Overall | 2130 | 47 | 35 | 39 | 28 | 43 | 23 | 17 | 81 | 100 | 6 | 76 | 19 |
| | Adm FIM cog ≤6 | 339 | 50 | 32 | 40 | 25 | 48 | 35 | 28 | 76 | 93 | 8 | 71 | 21 |
| | Adm FIM cog 7–10 | 374 | 52 | 34 | 42 | 26 | 48 | 27 | 23 | 77 | 94 | 3 | 85 | 12 |
| | Adm FIM cog 11–15 | 495 | 46 | 34 | 39 | 28 | 44 | 22 | 18 | 83 | 100 | 4 | 80 | 16 |
| | Adm FIM cog 16–20 | 408 | 46 | 38 | 41 | 33 | 43 | 19 | 15 | 87 | 100 | 4 | 73 | 22 |
| | Adm FIM cog ≥21 | 504 | 41 | 37 | 32 | 28 | 36 | 13 | 12 | 83 | 100 | 10 | 67 | 24 |
| Anticonvulsants: Ca+ channel antagonist | Overall | 2130 | 31 | 21 | 26 | 17 | 28 | 23 | 17 | 80 | 100 | 7 | 71 | 23 |
| | Adm FIM cog ≤6 | 339 | 30 | 19 | 25 | 15 | 29 | 36 | 29 | 75 | 90 | 10 | 67 | 22 |
| | Adm FIM cog 7–10 | 374 | 34 | 20 | 26 | 14 | 31 | 28 | 23 | 73 | 82 | 4 | 81 | 14 |
| | Adm FIM cog 11–15 | 495 | 29 | 19 | 25 | 17 | 28 | 22 | 19 | 81 | 100 | 4 | 74 | 22 |
| | Adm FIM cog 16–20 | 408 | 31 | 24 | 29 | 21 | 29 | 19 | 15 | 87 | 100 | 5 | 69 | 26 |
| | Adm FIM cog ≥21 | 504 | 29 | 24 | 25 | 20 | 25 | 13 | 12 | 85 | 100 | 10 | 61 | 29 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Anticonvulsants: GABA-A (agonist) | Overall | 2130 | >0 | >0 | >0 | >0 | 0 | 14 | 14 | 46 | 43 | 0 | 100 | 0 |
| | Adm FIM cog ≤6 | 339 | >0 | 0 | 0 | 0 | 0 | 23 | 23 | 26 | 26 | 0 | 100 | 0 |
| | Adm FIM cog 7–10 | 374 | >0 | 0 | 0 | 0 | 0 | 23 | 23 | 58 | 58 | 0 | 100 | 0 |
| | Adm FIM cog 11–15 | 495 | >0 | >0 | >0 | >0 | 0 | 5 | 5 | 71 | 71 | 0 | 100 | 0 |
| | Adm FIM cog ≥21 | 504 | >0 | 0 | 0 | 0 | 0 | 5 | 5 | 28 | 28 | 0 | 100 | 0 |
| Anticonvulsants: Na+ channel antagonist | Overall | 2130 | 25 | 17 | 18 | 12 | 22 | 21 | 16 | 73 | 91 | 5 | 82 | 13 |
| | Adm FIM cog ≤6 | 339 | 31 | 15 | 22 | 10 | 30 | 29 | 24 | 66 | 76 | 5 | 73 | 22 |
| | Adm FIM cog 7–10 | 374 | 31 | 18 | 24 | 13 | 28 | 23 | 20 | 69 | 78 | 4 | 88 | 8 |
| | Adm FIM cog 11–15 | 495 | 24 | 17 | 18 | 13 | 22 | 21 | 17 | 77 | 97 | 5 | 89 | 5 |
| | Adm FIM cog 16–20 | 408 | 23 | 19 | 18 | 14 | 21 | 18 | 14 | 81 | 100 | 3 | 79 | 18 |
| | Adm FIM cog ≥21 | 504 | 18 | 17 | 11 | 10 | 14 | 13 | 10 | 74 | 100 | 8 | 79 | 13 |
| Anticonvulsants: other | Overall | 2130 | >0 | >0 | >0 | >0 | 0 | 27 | 26 | 80 | 100 | 33 | 67 | 0 |
| | Adm FIM cog 7–10 | 374 | >0 | >0 | 0 | 0 | 0 | 11 | 11 | 39 | 39 | 100 | 0 | 0 |
| | Adm FIM cog 11–15 | 495 | >0 | >0 | >0 | >0 | 0 | 44 | 44 | 100 | 100 | 0 | 100 | 0 |
| | Adm FIM cog 16–20 | 408 | >0 | >0 | >0 | >0 | 0 | 26 | 26 | 100 | 100 | 0 | 100 | 0 |
| Antidepressants | Overall | 2130 | 67 | 44 | 55 | 37 | 61 | 23 | 18 | 78 | 93 | 27 | 60 | 13 |
| | Adm FIM cog ≤6 | 339 | 77 | 47 | 64 | 40 | 73 | 34 | 29 | 79 | 94 | 23 | 62 | 15 |
| | Adm FIM cog 7–10 | 374 | 76 | 48 | 63 | 39 | 72 | 26 | 22 | 78 | 90 | 25 | 65 | 10 |
| | Adm FIM cog 11–15 | 495 | 66 | 46 | 54 | 38 | 60 | 21 | 19 | 80 | 95 | 30 | 57 | 13 |
| | Adm FIM cog 16–20 | 408 | 69 | 49 | 58 | 42 | 62 | 17 | 14 | 78 | 95 | 28 | 57 | 15 |
| | Adm FIM cog ≥21 | 504 | 53 | 35 | 41 | 28 | 42 | 15 | 12 | 74 | 90 | 30 | 57 | 13 |
| Antidepressants: NDRI | Overall | 2130 | 1 | >0 | 1 | >0 | 1 | 12 | 10 | 69 | 87 | 7 | 83 | 10 |
| | Adm FIM cog ≤6 | 339 | >0 | >0 | >0 | >0 | 0 | 28 | 29 | 84 | 100 | 0 | 100 | 0 |
| | Adm FIM cog 7–10 | 374 | 1 | >0 | >0 | >0 | 0 | 15 | 10 | 54 | 54 | 0 | 75 | 25 |
| | Adm FIM cog 11–15 | 495 | 1 | >0 | 1 | >0 | 1 | 11 | 9 | 58 | 40 | 0 | 86 | 14 |
| | Adm FIM cog 16–20 | 408 | >0 | >0 | >0 | >0 | 0 | 9 | 10 | 73 | 92 | 33 | 67 | 0 |
| | Adm FIM cog ≥21 | 504 | 2 | 2 | 2 | 1 | 2 | 9 | 8 | 74 | 94 | 5 | 86 | 8 |
| Antidepressants: NaSSA | Overall | 2130 | 3 | >0 | 3 | >0 | 3 | 21 | 16 | 57 | 64 | 9 | 76 | 15 |
| | Adm FIM cog ≤6 | 339 | 5 | >0 | 4 | >0 | 4 | 16 | 14 | 36 | 30 | 13 | 52 | 35 |
| | Adm FIM cog 7–10 | 374 | 5 | 1 | 4 | >0 | 5 | 33 | 32 | 67 | 82 | 5 | 84 | 11 |
| | Adm FIM cog 11–15 | 495 | 2 | >0 | 2 | >0 | 2 | 19 | 16 | 57 | 62 | 8 | 83 | 8 |
| | Adm FIM cog 16–20 | 408 | 4 | 2 | 3 | 1 | 3 | 12 | 12 | 62 | 68 | 13 | 77 | 11 |
| | Adm FIM cog ≥21 | 504 | >0 | >0 | >0 | >0 | >0 | 22 | 20 | 84 | 86 | 0 | 100 | 0 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antidepressants: SARI | Overall | 2130 | 53 | 35 | 36 | 25 | 45 | 20 | 16 | 70 | 83 | 39 | 50 | 11 |
| | Adm FIM cog ≤6 | 339 | 63 | 40 | 42 | 30 | 57 | 30 | 26 | 73 | 90 | 31 | 58 | 11 |
| | Adm FIM cog 7–10 | 374 | 62 | 40 | 42 | 27 | 57 | 23 | 20 | 70 | 81 | 36 | 54 | 10 |
| | Adm FIM cog 11–15 | 495 | 54 | 36 | 37 | 27 | 47 | 19 | 17 | 72 | 89 | 41 | 49 | 10 |
| | Adm FIM cog 16–20 | 408 | 53 | 37 | 37 | 27 | 45 | 15 | 13 | 71 | 83 | 41 | 47 | 13 |
| | Adm FIM cog ≥21 | 504 | 37 | 25 | 25 | 16 | 27 | 11 | 9 | 64 | 72 | 47 | 41 | 12 |
| Antidepressants: SNRI | Overall | 2130 | 5 | 2 | 4 | 2 | 4 | 19 | 16 | 67 | 73 | 4 | 79 | 17 |
| | Adm FIM cog ≤6 | 339 | 4 | 1 | 4 | 1 | 4 | 26 | 24 | 59 | 50 | 10 | 69 | 21 |
| | Adm FIM cog 7–10 | 374 | 4 | >0 | 4 | >0 | 4 | 27 | 20 | 68 | 68 | >0 | 89 | 11 |
| | Adm FIM cog 11–15 | 495 | 5 | 1 | 4 | 1 | 4 | 18 | 19 | 60 | 71 | 4 | 74 | 22 |
| | Adm FIM cog 16–20 | 408 | 6 | 3 | 5 | 3 | 5 | 14 | 13 | 74 | 81 | 2 | 86 | 12 |
| | Adm FIM cog ≥21 | 504 | 4 | 2 | 4 | 1 | 4 | 13 | 10 | 71 | 81 | 5 | 75 | 20 |
| Antidepressants: SSRI | Overall | 2130 | 26 | 12 | 24 | 10 | 25 | 23 | 18 | 74 | 84 | 2 | 79 | 19 |
| | Adm FIM cog ≤6 | 339 | 32 | 9 | 29 | 6 | 31 | 32 | 27 | 65 | 66 | 4 | 70 | 26 |
| | Adm FIM cog 7–10 | 374 | 31 | 13 | 29 | 11 | 29 | 26 | 22 | 70 | 77 | 2 | 83 | 15 |
| | Adm FIM cog 11–15 | 495 | 24 | 12 | 23 | 11 | 24 | 22 | 18 | 79 | 93 | >0 | 80 | 19 |
| | Adm FIM cog 16–20 | 408 | 27 | 13 | 25 | 13 | 25 | 18 | 15 | 77 | 92 | 2 | 80 | 18 |
| | Adm FIM cog ≥21 | 504 | 19 | 11 | 16 | 10 | 17 | 19 | 15 | 81 | 95 | 3 | 82 | 15 |
| Antidepressants: TCA—secondary amines | Overall | 2130 | 2 | >0 | >0 | >0 | 2 | 21 | 13 | 55 | 55 | 7 | 76 | 18 |
| | Adm FIM cog ≤6 | 339 | 3 | 0 | 1 | 0 | 2 | 22 | 23 | 54 | 55 | 5 | 53 | 42 |
| | Adm FIM cog 7–10 | 374 | 1 | 0 | >0 | 0 | 0 | 18 | 16 | 41 | 36 | 0 | 100 | 0 |
| | Adm FIM cog 11–15 | 495 | 1 | >0 | >0 | >0 | 1 | 21 | 12 | 60 | 67 | 0 | 86 | 14 |
| | Adm FIM cog 16–20 | 408 | 1 | >0 | >0 | >0 | 1 | 6 | 7 | 47 | 45 | 4 | 66 | 30 |
| | Adm FIM cog ≥21 | 504 | 2 | >0 | >0 | >0 | 2 | 29 | 26 | 65 | 63 | 18 | 82 | 0 |
| Antidepressants: TCA—tertiary amines | Overall | 2130 | 3 | >0 | 2 | >0 | 3 | 16 | 14 | 62 | 67 | 5 | 72 | 23 |
| | Adm FIM cog ≤6 | 339 | 4 | >0 | 3 | >0 | 4 | 20 | 17 | 53 | 54 | 0 | 73 | 27 |
| | Adm FIM cog 7–10 | 374 | 3 | >0 | 2 | >0 | 3 | 14 | 11 | 53 | 54 | 11 | 73 | 17 |
| | Adm FIM cog 11–15 | 495 | 2 | >0 | 2 | >0 | 2 | 13 | 10 | 55 | 55 | 8 | 58 | 33 |
| | Adm FIM cog 16–20 | 408 | 4 | 2 | 3 | 1 | 4 | 16 | 14 | 71 | 77 | 0 | 81 | 19 |
| | Adm FIM cog ≥21 | 504 | 2 | >0 | 2 | >0 | 2 | 16 | 14 | 76 | 82 | 11 | 67 | 22 |
| Antiparkinson | Overall | 2130 | 25 | 11 | 20 | 8 | 23 | 25 | 21 | 73 | 83 | 3 | 83 | 14 |
| | Adm FIM cog ≤6 | 339 | 53 | 24 | 40 | 17 | 49 | 30 | 26 | 70 | 79 | 4 | 84 | 12 |
| | Adm FIM cog 7–10 | 374 | 40 | 18 | 31 | 13 | 36 | 25 | 22 | 71 | 85 | 1 | 87 | 12 |
| | Adm FIM cog 11–15 | 495 | 21 | 8 | 19 | 7 | 20 | 24 | 19 | 78 | 86 | 2 | 82 | 15 |
| | Adm FIM cog 16–20 | 408 | 15 | 4 | 12 | 4 | 13 | 16 | 14 | 71 | 75 | 5 | 72 | 23 |
| | Adm FIM cog ≥21 | 504 | 6 | 4 | 6 | 3 | 5 | 14 | 14 | 80 | 100 | 5 | 73 | 23 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antiparkinson: COMT inhibitor | Overall | 2130 | >0 | >0 | >0 | >0 | 0 | 23 | 23 | 100 | 100 | 4 | 96 | 0 |
| | Adm FIM cog ≤6 | 339 | >0 | >0 | >0 | >0 | 0 | 23 | 23 | 100 | 100 | 4 | 96 | 0 |
| Antiparkinson: DA agonist | Overall | 2130 | 9 | 4 | 7 | 2 | 9 | 25 | 21 | 71 | 81 | >0 | 89 | 10 |
| | Adm FIM cog ≤6 | 339 | 19 | 9 | 11 | 4 | 19 | 27 | 24 | 64 | 72 | >0 | 86 | 13 |
| | Adm FIM cog 7–10 | 374 | 16 | 6 | 12 | 4 | 15 | 29 | 23 | 71 | 84 | 0 | 91 | 9 |
| | Adm FIM cog 11–15 | 495 | 9 | 3 | 7 | 2 | 8 | 24 | 19 | 79 | 84 | 0 | 97 | 3 |
| | Adm FIM cog 16–20 | 408 | 5 | 1 | 4 | >0 | 4 | 14 | 11 | 68 | 75 | 0 | 80 | 20 |
| | Adm FIM cog ≥21 | 504 | 2 | 1 | 2 | 1 | 2 | 16 | 14 | 93 | 100 | 0 | 89 | 11 |
| Antiparkinson: MAO inhibitor | Overall | 2130 | >0 | >0 | >0 | >0 | >0 | 20 | 16 | 59 | 49 | >0 | 63 | 37 |
| | Adm FIM cog ≤6 | 339 | 1 | 0 | >0 | 0 | 0 | 24 | 25 | 25 | 25 | 0 | 25 | 75 |
| | Adm FIM cog 7–10 | 374 | 2 | 1 | 1 | >0 | 1 | 13 | 10 | 49 | 33 | 2 | 84 | 14 |
| | Adm FIM cog 11–15 | 495 | >0 | >0 | >0 | >0 | 0 | 34 | 21 | 88 | 100 | 0 | 33 | 67 |
| | Adm FIM cog 16–20 | 408 | >0 | >0 | >0 | >0 | 0 | 11 | 14 | 70 | 100 | 0 | 67 | 33 |
| | Adm FIM cog ≥21 | 504 | >0 | >0 | >0 | >0 | 0 | 25 | 25 | 100 | 100 | 0 | 100 | 0 |
| Antiparkinson: NMDA antagonist | Overall | 2130 | 17 | 6 | 13 | 5 | 15 | 24 | 19 | 66 | 71 | 4 | 81 | 15 |
| | Adm FIM cog ≤6 | 339 | 42 | 17 | 31 | 11 | 37 | 29 | 24 | 66 | 75 | 4 | 86 | 10 |
| | Adm FIM cog 7–10 | 374 | 25 | 10 | 19 | 7 | 22 | 22 | 18 | 64 | 66 | 2 | 85 | 13 |
| | Adm FIM cog 11–15 | 495 | 13 | 5 | 11 | 4 | 12 | 21 | 16 | 70 | 73 | 4 | 76 | 20 |
| | Adm FIM cog 16–20 | 408 | 9 | 2 | 6 | 2 | 8 | 16 | 12 | 65 | 64 | 8 | 69 | 24 |
| | Adm FIM cog ≥21 | 504 | 4 | 2 | 4 | 1 | 3 | 11 | 12 | 67 | 65 | 7 | 64 | 29 |
| Antiparkinson: other | Overall | 2130 | 1 | >0 | 1 | >0 | 1 | 27 | 20 | 74 | 100 | 3 | 84 | 13 |
| | Adm FIM cog ≤6 | 339 | 2 | 1 | 1 | >0 | 2 | 38 | 9 | 57 | 66 | 11 | 61 | 29 |
| | Adm FIM cog 7–10 | 374 | 3 | >0 | 2 | >0 | 3 | 25 | 19 | 70 | 70 | >0 | 100 | 0 |
| | Adm FIM cog 11–15 | 495 | 1 | >0 | 1 | >0 | 1 | 23 | 24 | 77 | 100 | 0 | 100 | 0 |
| | Adm FIM cog 16–20 | 408 | 1 | >0 | 1 | >0 | 1 | 24 | 22 | 93 | 100 | 0 | 60 | 40 |
| | Adm FIM cog ≥21 | 504 | >0 | >0 | >0 | >0 | 0 | 22 | 22 | 100 | 100 | 0 | 100 | 0 |
| Antipsychotic | Overall | 2130 | 25 | 16 | 15 | 10 | 21 | 20 | 15 | 65 | 75 | 23 | 62 | 15 |
| | Adm FIM cog ≤6 | 339 | 38 | 18 | 23 | 10 | 34 | 27 | 20 | 57 | 55 | 29 | 49 | 22 |
| | Adm FIM cog 7–10 | 374 | 34 | 21 | 23 | 13 | 30 | 21 | 17 | 66 | 78 | 24 | 61 | 15 |
| | Adm FIM cog 11–15 | 495 | 28 | 21 | 18 | 13 | 23 | 18 | 15 | 71 | 89 | 18 | 74 | 8 |
| | Adm FIM cog 16–20 | 408 | 22 | 16 | 11 | 7 | 18 | 15 | 13 | 63 | 75 | 17 | 71 | 12 |
| | Adm FIM cog ≥21 | 504 | 10 | 8 | 6 | 5 | 7 | 12 | 9 | 65 | 70 | 33 | 50 | 16 |
| Antipsychotic: first generation/typical | Overall | 2130 | 3 | 1 | >0 | >0 | >0 | 7 | 1 | 21 | 7 | 47 | 39 | 14 |
| | Adm FIM cog ≤6 | 339 | 3 | 2 | >0 | 0 | 0 | 7 | 2 | 12 | 4 | 49 | 37 | 14 |
| | Adm FIM cog 7–10 | 374 | 3 | 1 | >0 | 0 | 0 | 4 | 1 | 11 | 4 | 62 | 23 | 15 |
| | Adm FIM cog 11–15 | 495 | 3 | 2 | 1 | >0 | 1 | 12 | 2 | 34 | 21 | 41 | 47 | 13 |
| | Adm FIM cog 16–20 | 408 | 2 | >0 | >0 | >0 | 0 | 5 | 1 | 21 | 7 | 29 | 64 | 7 |
| | Adm FIM cog ≥21 | 504 | 1 | >0 | >0 | >0 | 0 | 5 | 1 | 28 | 10 | 49 | 30 | 21 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Antipsychotic: second generation/atypical | Overall | 2130 | 24 | 15 | 15 | 9 | 21 | 20 | 15 | 67 | 78 | 22 | 63 | 15 |
| | Adm FIM cog ≤6 | 339 | 37 | 16 | 22 | 9 | 33 | 27 | 20 | 58 | 56 | 29 | 48 | 23 |
| | Adm FIM cog 7–10 | 374 | 33 | 20 | 23 | 13 | 30 | 22 | 18 | 68 | 79 | 22 | 63 | 15 |
| | Adm FIM cog 11–15 | 495 | 26 | 19 | 17 | 13 | 22 | 18 | 16 | 74 | 92 | 15 | 76 | 9 |
| | Adm FIM cog 16–20 | 408 | 21 | 15 | 11 | 7 | 17 | 15 | 13 | 65 | 75 | 17 | 71 | 12 |
| | Adm FIM cog ≥21 | 504 | 9 | 7 | 6 | 4 | 7 | 13 | 11 | 71 | 79 | 31 | 53 | 15 |
| Hypnotic | Overall | 2130 | 30 | 14 | 20 | 10 | 23 | 18 | 13 | 60 | 67 | 48 | 42 | 10 |
| | Adm FIM cog ≤6 | 339 | 36 | 14 | 23 | 9 | 29 | 24 | 21 | 57 | 58 | 34 | 51 | 16 |
| | Adm FIM cog 7–10 | 374 | 37 | 17 | 26 | 12 | 31 | 22 | 18 | 62 | 70 | 41 | 50 | 9 |
| | Adm FIM cog 11–15 | 495 | 31 | 15 | 20 | 10 | 25 | 18 | 14 | 61 | 68 | 47 | 46 | 7 |
| | Adm FIM cog 16–20 | 408 | 25 | 13 | 16 | 8 | 16 | 11 | 9 | 57 | 64 | 55 | 35 | 9 |
| | Adm FIM cog ≥21 | 504 | 24 | 13 | 16 | 9 | 17 | 11 | 8 | 62 | 70 | 68 | 23 | 10 |
| Hypnotic: GABA-A agonist (benzodiazepine) | Overall | 2130 | 5 | 1 | 3 | >0 | 3 | 11 | 6 | 39 | 28 | 46 | 48 | 6 |
| | Adm FIM cog ≤6 | 339 | 4 | >0 | 2 | 0 | 2 | 10 | 7 | 25 | 20 | 39 | 55 | 7 |
| | Adm FIM cog 7–10 | 374 | 6 | >0 | 4 | >0 | 4 | 16 | 15 | 44 | 42 | 33 | 63 | 4 |
| | Adm FIM cog 11–15 | 495 | 5 | >0 | 3 | >0 | 3 | 13 | 10 | 46 | 36 | 36 | 64 | 0 |
| | Adm FIM cog 16–20 | 408 | 4 | 1 | 2 | >0 | 2 | 7 | 3 | 35 | 28 | 67 | 29 | 4 |
| | Adm FIM cog ≥21 | 504 | 4 | 2 | 2 | >0 | 1 | 6 | 2 | 39 | 25 | 61 | 24 | 14 |
| Hypnotic: GABA-A agonist (nonbenzodiazepine) | Overall | 2130 | 25 | 13 | 17 | 8 | 20 | 18 | 14 | 61 | 67 | 51 | 42 | 8 |
| | Adm FIM cog ≤6 | 339 | 30 | 12 | 19 | 7 | 26 | 25 | 23 | 60 | 67 | 35 | 52 | 13 |
| | Adm FIM cog 7–10 | 374 | 32 | 16 | 22 | 11 | 28 | 23 | 19 | 64 | 71 | 42 | 50 | 8 |
| | Adm FIM cog 11–15 | 495 | 26 | 13 | 15 | 8 | 20 | 17 | 14 | 59 | 63 | 54 | 42 | 4 |
| | Adm FIM cog 16–20 | 408 | 21 | 11 | 15 | 7 | 14 | 12 | 9 | 60 | 66 | 56 | 37 | 7 |
| | Adm FIM cog ≥21 | 504 | 19 | 11 | 13 | 8 | 15 | 12 | 8 | 64 | 71 | 70 | 23 | 7 |
| Hypnotic: melatonin agonist | Overall | 2130 | >0 | >0 | >0 | >0 | >0 | 18 | 10 | 54 | 47 | 8 | 54 | 38 |
| | Adm FIM cog ≤6 | 339 | 2 | >0 | 1 | >0 | 1 | 30 | 25 | 56 | 55 | 0 | 50 | 50 |
| | Adm FIM cog 7–10 | 374 | >0 | 0 | >0 | 0 | 0 | 12 | 12 | 71 | 71 | 0 | 100 | 0 |
| | Adm FIM cog 11–15 | 495 | >0 | >0 | >0 | 0 | 0 | 7 | 8 | 37 | 37 | 25 | 25 | 50 |
| | Adm FIM cog ≥21 | 504 | >0 | >0 | >0 | >0 | 0 | 10 | 10 | 73 | 73 | 0 | 100 | 0 |
| Hypnotic: other | Overall | 2130 | 3 | >0 | 2 | >0 | 2 | 16 | 5 | 43 | 25 | 39 | 34 | 27 |
| | Adm FIM cog ≤6 | 339 | 5 | 1 | 3 | >0 | 3 | 21 | 13 | 42 | 47 | 30 | 53 | 18 |
| | Adm FIM cog 7–10 | 374 | 3 | >0 | 2 | >0 | 2 | 19 | 13 | 50 | 65 | 46 | 38 | 15 |
| | Adm FIM cog 11–15 | 495 | 3 | >0 | 2 | >0 | 2 | 21 | 15 | 62 | 78 | 18 | 46 | 36 |
| | Adm FIM cog 16–20 | 408 | 2 | >0 | >0 | 0 | 0 | 4 | 2 | 17 | 11 | 50 | 13 | 38 |
| | Adm FIM cog ≥21 | 504 | 2 | >0 | >0 | >0 | 0 | 5 | 2 | 30 | 9 | 64 | 0 | 36 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Narcotic analgesic | Overall | 2130 | 72 | 55 | 45 | 36 | 59 | 16 | 13 | 65 | 77 | 63 | 26 | 11 |
| | Adm FIM cog ≤6 | 339 | 71 | 50 | 35 | 26 | 59 | 21 | 17 | 56 | 51 | 63 | 25 | 12 |
| | Adm FIM cog 7–10 | 374 | 74 | 50 | 40 | 29 | 60 | 18 | 14 | 57 | 59 | 61 | 30 | 9 |
| | Adm FIM cog 11–15 | 495 | 73 | 56 | 42 | 35 | 59 | 16 | 13 | 62 | 70 | 64 | 26 | 10 |
| | Adm FIM cog 16–20 | 408 | 75 | 60 | 51 | 43 | 60 | 14 | 12 | 69 | 90 | 57 | 32 | 12 |
| | Adm FIM cog ≥21 | 504 | 69 | 59 | 52 | 46 | 58 | 14 | 11 | 78 | 100 | 69 | 19 | 12 |
| Miscellaneous psychotropic | Overall | 2130 | 18 | 8 | 15 | 6 | 16 | 19 | 15 | 69 | 75 | 9 | 78 | 13 |
| | Adm FIM cog ≤6 | 339 | 24 | 4 | 22 | 3 | 23 | 26 | 21 | 58 | 59 | 16 | 76 | 8 |
| | Adm FIM cog 7–10 | 374 | 19 | 7 | 14 | 5 | 17 | 21 | 17 | 65 | 68 | 10 | 77 | 13 |
| | Adm FIM cog 11–15 | 495 | 21 | 10 | 17 | 8 | 20 | 17 | 16 | 73 | 81 | 4 | 84 | 12 |
| | Adm FIM cog 16–20 | 408 | 19 | 12 | 16 | 9 | 17 | 16 | 14 | 75 | 90 | 5 | 78 | 17 |
| | Adm FIM cog ≥21 | 504 | 10 | 7 | 7 | 6 | 8 | 13 | 9 | 72 | 98 | 14 | 69 | 18 |
| Miscellaneous psychotropic: AChEI | Overall | 2130 | 9 | 1 | 8 | 1 | 8 | 21 | 15 | 58 | 58 | 17 | 75 | 8 |
| | Adm FIM cog ≤6 | 339 | 18 | 1 | 17 | 1 | 17 | 26 | 20 | 54 | 56 | 21 | 73 | 6 |
| | Adm FIM cog 7–10 | 374 | 11 | 1 | 9 | 1 | 10 | 21 | 17 | 56 | 56 | 15 | 73 | 12 |
| | Adm FIM cog 11–15 | 495 | 10 | 2 | 9 | 2 | 9 | 16 | 13 | 63 | 65 | 9 | 85 | 6 |
| | Adm FIM cog 16–20 | 408 | 5 | 1 | 5 | 1 | 5 | 17 | 14 | 62 | 60 | 9 | 78 | 13 |
| | Adm FIM cog ≥21 | 504 | 2 | >0 | 2 | >0 | 2 | 15 | 10 | 61 | 50 | 57 | 33 | 10 |
| Miscellaneous psychotropic: NMDA antagonist | Overall | 2130 | 1 | >0 | 1 | >0 | 1 | 20 | 15 | 68 | 77 | 9 | 70 | 21 |
| | Adm FIM cog ≤6 | 339 | 2 | >0 | 2 | >0 | 2 | 33 | 16 | 64 | 65 | 18 | 40 | 43 |
| | Adm FIM cog 7–10 | 374 | 2 | >0 | >0 | >0 | 0 | 22 | 11 | 53 | 52 | 0 | 83 | 17 |
| | Adm FIM cog 11–15 | 495 | 2 | >0 | 2 | >0 | 1 | 16 | 18 | 79 | 89 | 3 | 72 | 24 |
| | Adm FIM cog 16–20 | 408 | 2 | >0 | 2 | >0 | 1 | 11 | 14 | 72 | 86 | 15 | 85 | 0 |
| Miscellaneous psychotropic: other | Overall | 2130 | 9 | 6 | 7 | 5 | 8 | 17 | 14 | 77 | 92 | 3 | 81 | 17 |
| | Adm FIM cog ≤6 | 339 | 5 | 2 | 4 | 1 | 5 | 24 | 21 | 71 | 79 | 0 | 90 | 10 |
| | Adm FIM cog 7–10 | 374 | 8 | 5 | 5 | 3 | 8 | 19 | 15 | 74 | 88 | 9 | 79 | 13 |
| | Adm FIM cog 11–15 | 495 | 11 | 8 | 8 | 5 | 11 | 19 | 17 | 80 | 95 | >0 | 83 | 16 |
| | Adm FIM cog 16–20 | 408 | 13 | 10 | 10 | 7 | 12 | 15 | 13 | 78 | 94 | 2 | 79 | 20 |
| | Adm FIM cog ≥21 | 504 | 8 | 7 | 6 | 5 | 6 | 12 | 10 | 75 | 100 | 3 | 78 | 19 |
| Stimulant | Overall | 2130 | 28 | 7 | 22 | 6 | 26 | 23 | 18 | 66 | 72 | 5 | 83 | 12 |
| | Adm FIM cog ≤6 | 339 | 57 | 16 | 41 | 12 | 54 | 29 | 27 | 67 | 75 | 4 | 79 | 17 |
| | Adm FIM cog 7–10 | 374 | 44 | 10 | 36 | 9 | 43 | 25 | 22 | 68 | 78 | 3 | 89 | 8 |
| | Adm FIM cog 11–15 | 495 | 25 | 5 | 20 | 4 | 23 | 19 | 16 | 63 | 64 | 5 | 84 | 11 |
| | Adm FIM cog 16–20 | 408 | 15 | 5 | 12 | 4 | 13 | 13 | 11 | 65 | 67 | 9 | 78 | 14 |
| | Adm FIM cog ≥21 | 504 | 8 | 2 | 7 | 2 | 6 | 11 | 9 | 64 | 64 | 10 | 79 | 10 |

(*continued on next page*)

**Supplemental Table S1** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | n* | % Ever Received | % Received First 2d | % Received Last 2d | % Received First and Last 2d | % Received ≥5d | Mean No. of Days (for Those Received) | Median No. of Days (for Those Received) | Mean % Stay (for Those Received) | Median % Stay (for Those Received) | % Days PRN | % Days Scheduled | % Days Unknown PRN/ Scheduled |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Stimulant: NE agonist | Overall | 2130 | 3 | >0 | 2 | >0 | 2 | 23 | 17 | 56 | 57 | 0 | 92 | 8 |
| | Adm FIM cog ≤6 | 339 | 4 | >0 | 4 | >0 | 4 | 33 | 29 | 60 | 53 | 0 | 100 | 0 |
| | Adm FIM cog 7—10 | 374 | 6 | 0 | 5 | 0 | 5 | 22 | 23 | 57 | 72 | 0 | 94 | 6 |
| | Adm FIM cog 11—15 | 495 | 3 | >0 | 2 | >0 | 3 | 26 | 15 | 62 | 69 | 0 | 77 | 23 |
| | Adm FIM cog 16—20 | 408 | 1 | >0 | >0 | 0 | 0 | 5 | 6 | 36 | 27 | 0 | 100 | 0 |
| | Adm FIM cog ≥21 | 504 | >0 | >0 | >0 | 0 | 0 | 16 | 16 | 39 | 39 | 0 | 100 | 0 |
| Stimulant: NE-DA-5HT agonist | Overall | 2130 | 23 | 5 | 18 | 4 | 21 | 23 | 18 | 64 | 70 | 6 | 81 | 13 |
| | Adm FIM cog ≤6 | 339 | 51 | 11 | 38 | 8 | 48 | 28 | 27 | 64 | 72 | 5 | 77 | 18 |
| | Adm FIM cog 7—10 | 374 | 35 | 7 | 29 | 6 | 33 | 25 | 22 | 65 | 72 | 4 | 89 | 7 |
| | Adm FIM cog 11—15 | 495 | 21 | 4 | 17 | 3 | 19 | 19 | 16 | 61 | 62 | 6 | 82 | 12 |
| | Adm FIM cog 16—20 | 408 | 13 | 5 | 10 | 3 | 10 | 13 | 11 | 64 | 72 | 11 | 76 | 13 |
| | Adm FIM cog ≥21 | 504 | 6 | 2 | 5 | 2 | 5 | 11 | 10 | 63 | 64 | 10 | 75 | 14 |
| Stimulant: other | Overall | 2130 | 6 | 2 | 4 | 1 | 5 | 22 | 15 | 64 | 67 | 1 | 83 | 16 |
| | Adm FIM cog ≤6 | 339 | 11 | 6 | 4 | 3 | 10 | 29 | 18 | 57 | 49 | 0 | 69 | 31 |
| | Adm FIM cog 7—10 | 374 | 10 | 3 | 9 | 2 | 10 | 25 | 22 | 72 | 86 | >0 | 84 | 15 |
| | Adm FIM cog 11—15 | 495 | 4 | 1 | 3 | >0 | 3 | 16 | 10 | 60 | 61 | >0 | 100 | 0 |
| | Adm FIM cog 16—20 | 408 | 3 | >0 | 2 | >0 | 2 | 12 | 9 | 60 | 56 | 0 | 82 | 18 |
| | Adm FIM cog ≥21 | 504 | 2 | >0 | 2 | >0 | 1 | 9 | 6 | 59 | 50 | 11 | 89 | 0 |

Abbreviations: Adm FIM cog, admission FIM cognitive subscale; COMT, catechol-O-methyltransferase; DA, dopamine; GABA-A, gamma-aminobutyric acid-A; MAO, monoamine oxidase; NaSSA, noradrenergic and specific serotonergic antidepressant; NDRI, norepinephrine-dopamine reuptake inhibitor; NE, norepinephrine; NE-DA-5HT, norepinephrine-dopamine-5HT; NMDA, N-methyl-D-aspartate; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

* Ten patients were excluded because of missing admission FIM cognitive scores.

**Supplemental Table S2** Expanded psychoactive medication data by pharmaceutical class, week of rehabilitation, and level of cognitive function

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Sample size by week (n)* | Overall | 2130 | 2008 | 1551 | 1065 | 707 | 482 | 339 | 215 | 153 |
| | Adm FIM cog ≤6 | 339 | 333 | 323 | 288 | 223 | 160 | 107 | 79 | 59 |
| | Adm FIM cog 7–10 | 374 | 371 | 337 | 266 | 185 | 121 | 90 | 56 | 34 |
| | Adm FIM cog 11–15 | 495 | 482 | 387 | 236 | 127 | 73 | 48 | 30 | 27 |
| | Adm FIM cog 16–20 | 408 | 381 | 253 | 126 | 74 | 50 | 42 | 24 | 17 |
| | Adm FIM cog ≥21 | 504 | 432 | 242 | 140 | 91 | 71 | 47 | 23 | 16 |
| Anxiolytics (%) | Overall | 24 | 22 | 23 | 23 | 26 | 28 | 30 | 32 | 31 |
| | Adm FIM cog ≤6 | 31 | 30 | 29 | 30 | 30 | 29 | 30 | 33 | 27 |
| | Adm FIM cog 7–10 | 30 | 27 | 27 | 26 | 30 | 35 | 40 | 41 | 38 |
| | Adm FIM cog 11–15 | 24 | 23 | 21 | 20 | 24 | 29 | 29 | 30 | 37 |
| | Adm FIM cog 16–20 | 23 | 19 | 19 | 19 | 19 | 20 | 24 | 21 | 29 |
| | Adm FIM cog ≥21 | 16 | 14 | 14 | 13 | 14 | 15 | 15 | 22 | 19 |
| Anxiolytics: GABA-A (%) | Overall | 22 | 18 | 18 | 19 | 21 | 23 | 24 | 27 | 25 |
| | Adm FIM cog ≤6 | 29 | 26 | 24 | 26 | 25 | 24 | 25 | 28 | 22 |
| | Adm FIM cog 7–10 | 29 | 24 | 23 | 22 | 25 | 27 | 31 | 34 | 32 |
| | Adm FIM cog 11–15 | 20 | 19 | 17 | 17 | 19 | 23 | 25 | 23 | 26 |
| | Adm FIM cog 16–20 | 19 | 14 | 15 | 13 | 14 | 18 | 19 | 21 | 29 |
| | Adm FIM cog ≥21 | 14 | 11 | 10 | 8 | 11 | 13 | 11 | 17 | 19 |
| Anxiolytic: H1 (%) | Overall | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 |
| | Adm FIM cog ≤6 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 7–10 | >0 | >0 | >0 | >0 | 1 | 2 | 2 | 2 | 3 |
| | Adm FIM cog 11–15 | 0 | >0 | >0 | 0 | >0 | 1 | 0 | 0 | 0 |
| | Adm FIM cog 16–20 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| Anxiolytic: other (%) | Overall | 4 | 5 | 6 | 7 | 8 | 9 | 9 | 9 | 10 |
| | Adm FIM cog ≤6 | 3 | 5 | 7 | 8 | 9 | 9 | 11 | 11 | 12 |
| | Adm FIM cog 7–10 | 5 | 6 | 7 | 7 | 9 | 11 | 11 | 9 | 9 |
| | Adm FIM cog 11–15 | 5 | 5 | 6 | 6 | 9 | 11 | 8 | 10 | 15 |
| | Adm FIM cog 16–20 | 5 | 6 | 5 | 8 | 8 | 6 | 10 | 4 | 6 |
| | Adm FIM cog ≥21 | 2 | 3 | 4 | 5 | 3 | 3 | 4 | 4 | 0 |
| Anticonvulsant (%) | Overall | 39 | 39 | 39 | 41 | 42 | 43 | 42 | 46 | 48 |
| | Adm FIM cog ≤6 | 37 | 38 | 38 | 42 | 41 | 45 | 43 | 49 | 59 |
| | Adm FIM cog 7–10 | 39 | 39 | 41 | 45 | 52 | 52 | 51 | 52 | 53 |
| | Adm FIM cog 11–15 | 38 | 40 | 41 | 43 | 46 | 48 | 46 | 50 | 52 |
| | Adm FIM cog 16–20 | 41 | 41 | 40 | 41 | 49 | 44 | 40 | 29 | 24 |
| | Adm FIM cog ≥21 | 39 | 34 | 31 | 23 | 12 | 13 | 13 | 22 | 19 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Anticonvulsant: Ca+ channel antagonist (%) | Overall | 24 | 25 | 26 | 27 | 29 | 29 | 29 | 30 | 31 |
| | Adm FIM cog ≤6 | 23 | 23 | 23 | 25 | 26 | 30 | 28 | 29 | 37 |
| | Adm FIM cog 7–10 | 23 | 25 | 28 | 31 | 36 | 36 | 38 | 38 | 35 |
| | Adm FIM cog 11-15 | 21 | 25 | 27 | 29 | 31 | 36 | 31 | 33 | 33 |
| | Adm FIM cog 16–20 | 26 | 29 | 28 | 30 | 38 | 30 | 26 | 17 | 18 |
| | Adm FIM cog ≥21 | 25 | 24 | 21 | 17 | 8 | 7 | 4 | 13 | 6 |
| Anticonvulsant: GABA-A (agonist) (%) | Overall | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 | 0 |
| | Adm FIM cog ≤6 | 0 | 0 | 0 | 0 | >0 | >0 | >0 | 1 | 0 |
| | Adm FIM cog 7–10 | 0 | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | >0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Anticonvulsant: Na+ channel antagonist (%) | Overall | 19 | 19 | 19 | 20 | 21 | 22 | 23 | 27 | 31 |
| | Adm FIM cog ≤6 | 19 | 20 | 20 | 22 | 20 | 22 | 24 | 29 | 34 |
| | Adm FIM cog 7–10 | 21 | 22 | 23 | 24 | 28 | 27 | 22 | 25 | 35 |
| | Adm FIM cog 11–15 | 19 | 19 | 18 | 21 | 24 | 26 | 27 | 33 | 33 |
| | Adm FIM cog 16–20 | 21 | 20 | 17 | 18 | 23 | 30 | 31 | 25 | 24 |
| | Adm FIM cog ≥21 | 17 | 13 | 13 | 10 | 7 | 7 | 11 | 13 | 13 |
| Anticonvulsant: other (%) | Overall | >0 | >0 | >0 | >0 | >0 | >0 | >0 | 0 | 0 |
| | Adm FIM cog 7–10 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | >0 | >0 | >0 | >0 | >0 | 1 | 2 | 0 | 0 |
| | Adm FIM cog 16–20 | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |
| Antidepressant (%) | Overall | 56 | 59 | 62 | 65 | 66 | 67 | 66 | 67 | 69 |
| | Adm FIM cog ≤6 | 59 | 65 | 65 | 68 | 71 | 72 | 71 | 63 | 73 |
| | Adm FIM cog 7–10 | 61 | 65 | 69 | 68 | 71 | 72 | 74 | 70 | 62 |
| | Adm FIM cog 11–15 | 58 | 59 | 62 | 67 | 61 | 63 | 65 | 73 | 78 |
| | Adm FIM cog 16–20 | 60 | 63 | 64 | 64 | 68 | 60 | 52 | 63 | 59 |
| | Adm FIM cog ≥21 | 44 | 47 | 47 | 48 | 51 | 54 | 53 | 65 | 63 |
| Antidepressant: NDRI (%) | Overall | 1 | 1 | >0 | >0 | >0 | >0 | >0 | >0 | 0 |
| | Adm FIM cog ≤6 | >0 | >0 | >0 | >0 | >0 | >0 | >0 | 1 | 0 |
| | Adm FIM cog 7–10 | >0 | >0 | >0 | >0 | 1 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | >0 | 1 | 1 | 0 | 0 | 1 | 2 | 0 | 0 |
| | Adm FIM cog 16–20 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | 2 | 2 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |
| Antidepressant: NaSSA (%) | Overall | 2 | 2 | 3 | 3 | 3 | 4 | 6 | 7 | 7 |
| | Adm FIM cog ≤6 | 1 | 2 | 2 | 3 | 4 | 4 | 5 | 3 | 3 |
| | Adm FIM cog 7–10 | 3 | 4 | 4 | 4 | 5 | 7 | 11 | 16 | 15 |
| | Adm FIM cog 11–15 | 1 | 1 | 2 | 2 | 0 | 1 | 2 | 7 | 7 |
| | Adm FIM cog 16–20 | 2 | 3 | 4 | 2 | 1 | 2 | 5 | 4 | 6 |
| | Adm FIM cog ≥21 | >0 | 1 | 2 | 3 | 3 | 0 | 0 | 0 | 0 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Antidepressant: SARI (%) | Overall | 45 | 46 | 48 | 48 | 47 | 47 | 43 | 42 | 39 |
| | Adm FIM cog ≤6 | 52 | 54 | 55 | 55 | 53 | 53 | 49 | 43 | 46 |
| | Adm FIM cog 7–10 | 52 | 51 | 55 | 52 | 53 | 55 | 53 | 43 | 32 |
| | Adm FIM cog 11–15 | 47 | 47 | 48 | 50 | 44 | 48 | 50 | 53 | 52 |
| | Adm FIM cog 16–20 | 48 | 46 | 46 | 47 | 49 | 40 | 29 | 42 | 35 |
| | Adm FIM cog ≥21 | 32 | 31 | 28 | 24 | 19 | 21 | 17 | 13 | 6 |
| Antidepressant: SNRI (%) | Overall | 2 | 3 | 3 | 4 | 4 | 5 | 4 | 5 | 3 |
| | Adm FIM cog ≤6 | 1 | 2 | 2 | 3 | 4 | 4 | 4 | 4 | 0 |
| | Adm FIM cog 7–10 | 2 | 2 | 4 | 3 | 3 | 4 | 6 | 7 | 9 |
| | Adm FIM cog 11–15 | 2 | 4 | 4 | 6 | 6 | 7 | 2 | 0 | 4 |
| | Adm FIM cog 16–20 | 4 | 5 | 5 | 3 | 4 | 4 | 5 | 4 | 0 |
| | Adm FIM cog ≥21 | 3 | 4 | 2 | 4 | 3 | 3 | 4 | 4 | 6 |
| Antidepressant: SSRI (%) | Overall | 16 | 20 | 23 | 26 | 30 | 32 | 34 | 38 | 42 |
| | Adm FIM cog ≤6 | 13 | 18 | 18 | 22 | 29 | 34 | 37 | 39 | 51 |
| | Adm FIM cog 7–10 | 17 | 21 | 25 | 30 | 32 | 36 | 39 | 36 | 32 |
| | Adm FIM cog 11–15 | 16 | 19 | 23 | 27 | 29 | 29 | 33 | 37 | 37 |
| | Adm FIM cog 16–20 | 18 | 25 | 26 | 29 | 34 | 30 | 26 | 29 | 29 |
| | Adm FIM cog ≥21 | 14 | 17 | 20 | 21 | 24 | 28 | 28 | 48 | 50 |
| Antidepressant: TCA—secondary amines (%) | Overall | >0 | >0 | 1 | 1 | 2 | 2 | 3 | 4 | 5 |
| | Adm FIM cog ≤6 | >0 | 1 | 2 | 2 | 2 | 3 | 3 | 4 | 5 |
| | Adm FIM cog 7–10 | >0 | >0 | >0 | >0 | 1 | 0 | 0 | 2 | 3 |
| | Adm FIM cog 11–15 | 1 | >0 | >0 | >0 | >0 | 1 | 2 | 3 | 4 |
| | Adm FIM cog 16–20 | >0 | 0 | >0 | >0 | 1 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | 2 | 2 | 4 | 7 | 7 | 11 | 13 | 13 |
| Antidepressant: TCA—tertiary amines (%) | Overall | 2 | 2 | 3 | 3 | 3 | 2 | 1 | 1 | 3 |
| | Adm FIM cog ≤6 | 1 | 2 | 2 | 3 | 3 | 2 | 3 | 3 | 3 |
| | Adm FIM cog 7–10 | 1 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | 2 | 2 | 2 | 2 | 2 | 3 | 0 | 0 | 0 |
| | Adm FIM cog 16–20 | 3 | 3 | 4 | 5 | 4 | 2 | 2 | 4 | 6 |
| | Adm FIM cog ≥21 | >0 | 2 | 2 | 3 | 2 | 3 | 0 | 0 | 6 |
| Antiparkinson (%) | Overall | 16 | 21 | 25 | 29 | 32 | 32 | 32 | 31 | 27 |
| | Adm FIM cog ≤6 | 35 | 41 | 41 | 44 | 44 | 45 | 45 | 42 | 36 |
| | Adm FIM cog 7–10 | 26 | 29 | 32 | 35 | 38 | 42 | 43 | 39 | 32 |
| | Adm FIM cog 11–15 | 15 | 19 | 22 | 25 | 28 | 30 | 25 | 27 | 30 |
| | Adm FIM cog 16–20 | 9 | 14 | 15 | 18 | 18 | 12 | 14 | 13 | 12 |
| | Adm FIM cog ≥21 | 4 | 6 | 7 | 6 | 4 | 3 | 0 | 0 | 0 |
| Antiparkinson: COMT inhibitor (%) | Overall | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≤6 | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Antiparkinson: DA agonist (%) | Overall | 6 | 8 | 9 | 11 | 13 | 13 | 12 | 11 | 11 |
| | Adm FIM cog ≤6 | 12 | 15 | 14 | 15 | 16 | 15 | 14 | 14 | 14 |
| | Adm FIM cog 7–10 | 9 | 12 | 13 | 15 | 18 | 21 | 21 | 16 | 18 |
| | Adm FIM cog 11–15 | 7 | 8 | 8 | 10 | 12 | 15 | 13 | 10 | 11 |
| | Adm FIM cog 16–20 | 4 | 5 | 4 | 7 | 5 | 2 | 2 | 0 | 0 |
| | Adm FIM cog ≥21 | 2 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| Antiparkinson: MAO inhibitor (%) | Overall | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 |
| | Adm FIM cog ≤6 | 0 | >0 | >0 | >0 | >0 | 1 | >0 | 1 | 0 |
| | Adm FIM cog 7–10 | 1 | >0 | >0 | 1 | 2 | 2 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | >0 | >0 | >0 | 0 | 0 | 0 | 2 | 3 | 4 |
| | Adm FIM cog 16–20 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | >0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Antiparkinson: NMDA antagonist (%) | Overall | 10 | 13 | 16 | 19 | 20 | 21 | 21 | 22 | 18 |
| | Adm FIM cog ≤6 | 26 | 31 | 31 | 33 | 32 | 33 | 36 | 34 | 29 |
| | Adm FIM cog 7–10 | 15 | 17 | 19 | 19 | 19 | 21 | 22 | 21 | 15 |
| | Adm FIM cog 11–15 | 7 | 10 | 12 | 14 | 15 | 16 | 10 | 13 | 15 |
| | Adm FIM cog 16–20 | 4 | 8 | 10 | 10 | 11 | 10 | 12 | 13 | 12 |
| | Adm FIM cog ≥21 | 2 | 3 | 4 | 3 | 3 | 3 | 0 | 0 | 0 |
| Antiparkinson: other (%) | Overall | >0 | 1 | 1 | 1 | 2 | >0 | >0 | >0 | 1 |
| | Adm FIM cog ≤6 | 1 | 1 | 1 | >0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 7–10 | 1 | 2 | 2 | 2 | 3 | 2 | 3 | 4 | 6 |
| | Adm FIM cog 11–15 | >0 | 1 | 1 | >0 | 2 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 16–20 | >0 | 1 | 2 | 2 | 4 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | >0 | >0 | 1 | 1 | 0 | 0 | 0 |
| Antipsychotic (%) | Overall | 20 | 19 | 19 | 20 | 21 | 22 | 23 | 24 | 29 |
| | Adm FIM cog ≤6 | 25 | 24 | 24 | 27 | 27 | 30 | 33 | 35 | 42 |
| | Adm FIM cog 7–10 | 26 | 25 | 23 | 23 | 23 | 25 | 27 | 27 | 29 |
| | Adm FIM cog 11–15 | 24 | 21 | 20 | 21 | 19 | 15 | 17 | 17 | 26 |
| | Adm FIM cog 16–20 | 19 | 19 | 19 | 15 | 16 | 18 | 17 | 8 | 6 |
| | Adm FIM cog ≥21 | 9 | 7 | 8 | 7 | 7 | 7 | 6 | 4 | 6 |
| Antipsychotic: first generation/ typical (%) | Overall | 2 | >0 | >0 | >0 | 1 | >0 | >0 | >0 | 3 |
| | Adm FIM cog ≤6 | 2 | 0 | 0 | >0 | >0 | >0 | 0 | 0 | 2 |
| | Adm FIM cog 7–10 | 2 | >0 | >0 | >0 | 2 | 0 | 0 | 2 | 3 |
| | Adm FIM cog 11–15 | 2 | 1 | 2 | >0 | >0 | 1 | 2 | 3 | 7 |
| | Adm FIM cog 16–20 | 2 | >0 | >0 | >0 | 1 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Antipsychotic: second generation/atypical (%) | Overall | 19 | 19 | 19 | 20 | 20 | 22 | 22 | 23 | 26 |
| | Adm FIM cog ≤6 | 23 | 24 | 24 | 26 | 26 | 30 | 33 | 35 | 41 |
| | Adm FIM cog 7–10 | 25 | 25 | 22 | 22 | 22 | 25 | 27 | 25 | 26 |
| | Adm FIM cog 11–15 | 22 | 20 | 19 | 20 | 19 | 15 | 15 | 13 | 19 |
| | Adm FIM cog 16–20 | 18 | 19 | 18 | 14 | 15 | 18 | 17 | 8 | 6 |
| | Adm FIM cog ≥21 | 8 | 7 | 7 | 6 | 7 | 7 | 6 | 4 | 6 |
| Hypnotic (%) | Overall | 21 | 22 | 24 | 26 | 26 | 26 | 25 | 25 | 27 |
| | Adm FIM cog ≤6 | 21 | 24 | 23 | 26 | 26 | 25 | 22 | 25 | 25 |
| | Adm FIM cog 7–10 | 25 | 26 | 29 | 32 | 30 | 34 | 33 | 34 | 38 |
| | Adm FIM cog 11–15 | 23 | 23 | 26 | 31 | 32 | 36 | 35 | 33 | 33 |
| | Adm FIM cog 16–20 | 18 | 18 | 19 | 18 | 18 | 12 | 10 | 0 | 6 |
| | Adm FIM cog ≥21 | 20 | 18 | 18 | 16 | 14 | 14 | 15 | 13 | 19 |
| Hypnotic: GABA-A agonist (benzodiazepine) (%) | Overall | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 4 | 5 |
| | Adm FIM cog ≤6 | 1 | 1 | 1 | 2 | 2 | 2 | >0 | 4 | 5 |
| | Adm FIM cog 7–10 | 2 | 3 | 3 | 5 | 5 | 5 | 7 | 5 | 6 |
| | Adm FIM cog 11–15 | 2 | 2 | 3 | 5 | 5 | 4 | 4 | 7 | 4 |
| | Adm FIM cog 16–20 | 2 | 2 | 2 | 2 | 3 | 4 | 2 | 0 | 6 |
| | Adm FIM cog ≥21 | 3 | 2 | 3 | 1 | 0 | 1 | 0 | 0 | 0 |
| Hypnotic: GABA-A agonist (nonbenzodiazepine) (%) | Overall | 18 | 19 | 21 | 23 | 23 | 22 | 22 | 21 | 23 |
| | Adm FIM cog ≤6 | 18 | 20 | 20 | 23 | 23 | 21 | 20 | 22 | 22 |
| | Adm FIM cog 7–10 | 21 | 22 | 26 | 28 | 26 | 30 | 28 | 30 | 38 |
| | Adm FIM cog 11–15 | 19 | 20 | 22 | 26 | 26 | 29 | 29 | 27 | 22 |
| | Adm FIM cog 16–20 | 16 | 16 | 17 | 17 | 16 | 10 | 10 | 0 | 0 |
| | Adm FIM cog ≥21 | 16 | 15 | 14 | 14 | 14 | 14 | 15 | 13 | 19 |
| Hypnotic: melatonin agonist (%) | Overall | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 | >0 |
| | Adm FIM cog ≤6 | >0 | 1 | 1 | 2 | 1 | 1 | >0 | 1 | 2 |
| | Adm FIM cog 7–10 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 11–15 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | >0 | >0 | >0 | 0 | 0 | 0 | 0 | 0 |
| Hypnotic: other (%) | Overall | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 6 |
| | Adm FIM cog ≤6 | 1 | 3 | 2 | 2 | 3 | 3 | 3 | 5 | 7 |
| | Adm FIM cog 7–10 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 3 |
| | Adm FIM cog 11–15 | 1 | 2 | 2 | 2 | 6 | 5 | 6 | 10 | 11 |
| | Adm FIM cog 16–20 | >0 | 1 | >0 | >0 | 0 | 0 | 0 | 0 | 6 |
| | Adm FIM cog ≥21 | 1 | 2 | 1 | >0 | 0 | 0 | 0 | 0 | 0 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Narcotic analgesic (%) | Overall | 65 | 60 | 55 | 49 | 49 | 45 | 40 | 42 | 40 |
| | Adm FIM cog ≤6 | 59 | 56 | 52 | 47 | 46 | 45 | 41 | 42 | 41 |
| | Adm FIM cog 7–10 | 63 | 59 | 52 | 47 | 50 | 48 | 44 | 48 | 38 |
| | Adm FIM cog 11–15 | 67 | 60 | 55 | 51 | 50 | 52 | 46 | 47 | 48 |
| | Adm FIM cog 16–20 | 69 | 63 | 58 | 52 | 54 | 36 | 31 | 25 | 29 |
| | Adm FIM cog ≥21 | 66 | 62 | 59 | 48 | 42 | 37 | 30 | 35 | 38 |
| Miscellaneous psychotropic (%) | Overall | 11 | 13 | 15 | 14 | 16 | 18 | 19 | 20 | 18 |
| | Adm FIM cog ≤6 | 6 | 10 | 15 | 19 | 20 | 23 | 27 | 28 | 25 |
| | Adm FIM cog 7–10 | 11 | 13 | 13 | 13 | 16 | 18 | 14 | 20 | 15 |
| | Adm FIM cog 11–15 | 14 | 16 | 18 | 16 | 16 | 15 | 23 | 23 | 19 |
| | Adm FIM cog 16–20 | 15 | 18 | 18 | 14 | 14 | 14 | 12 | 13 | 12 |
| | Adm FIM cog ≥21 | 8 | 8 | 7 | 6 | 7 | 10 | 9 | 4 | 0 |
| Miscellaneous psychotropic: AChEI (%) | Overall | 3 | 5 | 7 | 9 | 10 | 13 | 14 | 17 | 14 |
| | Adm FIM cog ≤6 | 2 | 6 | 10 | 14 | 15 | 21 | 25 | 25 | 24 |
| | Adm FIM cog 7–10 | 4 | 6 | 8 | 9 | 11 | 13 | 10 | 18 | 12 |
| | Adm FIM cog 11–15 | 4 | 6 | 8 | 8 | 9 | 11 | 17 | 17 | 11 |
| | Adm FIM cog 16–20 | 3 | 5 | 6 | 6 | 5 | 8 | 7 | 8 | 6 |
| | Adm FIM cog ≥21 | >0 | 2 | 2 | 3 | 2 | 3 | 2 | 0 | 0 |
| Miscellaneous psychotropic: NMDA antagonist (%) | Overall | >0 | >0 | 1 | >0 | >0 | >0 | >0 | 1 | 2 |
| | Adm FIM cog ≤6 | >0 | >0 | >0 | 1 | >0 | >0 | >0 | 1 | 2 |
| | Adm FIM cog 7–10 | >0 | 1 | >0 | >0 | 1 | 2 | 2 | 4 | 6 |
| | Adm FIM cog 11–15 | 1 | 1 | 2 | 1 | >0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog 16–20 | 1 | 2 | 2 | >0 | 0 | 0 | 0 | 0 | 0 |
| Miscellaneous psychotropic: other (%) | Overall | 8 | 8 | 7 | 5 | 6 | 5 | 4 | 3 | 3 |
| | Adm FIM cog ≤6 | 3 | 3 | 5 | 5 | 4 | 3 | 2 | 3 | 2 |
| | Adm FIM cog 7–10 | 7 | 8 | 6 | 4 | 5 | 6 | 3 | 0 | 0 |
| | Adm FIM cog 11–15 | 10 | 10 | 10 | 8 | 8 | 5 | 6 | 7 | 7 |
| | Adm FIM cog 16–20 | 12 | 12 | 11 | 9 | 8 | 6 | 5 | 4 | 6 |
| | Adm FIM cog ≥21 | 7 | 7 | 5 | 4 | 4 | 7 | 6 | 4 | 0 |
| Stimulant (%) | Overall | 15 | 21 | 27 | 33 | 38 | 39 | 38 | 35 | 34 |
| | Adm FIM cog ≤6 | 30 | 42 | 46 | 51 | 56 | 57 | 57 | 52 | 49 |
| | Adm FIM cog 7–10 | 25 | 33 | 38 | 43 | 44 | 51 | 49 | 45 | 38 |
| | Adm FIM cog 11–15 | 13 | 18 | 21 | 28 | 33 | 34 | 35 | 30 | 37 |
| | Adm FIM cog 16–20 | 9 | 13 | 13 | 11 | 14 | 6 | 5 | 0 | 0 |
| | Adm FIM cog ≥21 | 4 | 6 | 7 | 7 | 5 | 4 | 4 | 0 | 0 |

(*continued on next page*)

**Supplemental Table S2** (*continued*)

| Pharmaceutical Class by Mechanism | FIM Cognitive Score at Admission | Received Week 1 (admit) | Received Week 2 | Received Week 3 | Received Week 4 | Received Week 5 | Received Week 6 | Received Week 7 | Received Week 8 | Received Week 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Stimulant: NE agonist (%) | Overall | >0 | 1 | 2 | 3 | 4 | 4 | 5 | 7 | 7 |
| | Adm FIM cog ≤6 | 1 | 2 | 2 | 3 | 5 | 6 | 7 | 8 | 7 |
| | Adm FIM cog 7–10 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 9 |
| | Adm FIM cog 11–15 | 1 | 1 | 2 | 4 | 5 | 4 | 6 | 10 | 11 |
| | Adm FIM cog 16–20 | >0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | >0 | 0 | >0 | >0 | 1 | 1 | 2 | 0 | 0 |
| Stimulant: NE-DA-5HT agonist (%) | Overall | 11 | 17 | 22 | 28 | 32 | 34 | 33 | 31 | 31 |
| | Adm FIM cog ≤6 | 23 | 35 | 40 | 45 | 49 | 50 | 50 | 47 | 46 |
| | Adm FIM cog 7–10 | 17 | 25 | 28 | 33 | 36 | 45 | 43 | 43 | 35 |
| | Adm FIM cog 11–15 | 9 | 14 | 18 | 24 | 28 | 30 | 29 | 20 | 30 |
| | Adm FIM cog 16–20 | 7 | 10 | 12 | 11 | 12 | 6 | 5 | 0 | 0 |
| | Adm FIM cog ≥21 | 3 | 4 | 5 | 5 | 4 | 3 | 2 | 0 | 0 |
| Stimulant: other (%) | Overall | 4 | 5 | 5 | 5 | 6 | 7 | 6 | 9 | 8 |
| | Adm FIM cog ≤6 | 8 | 8 | 7 | 7 | 7 | 9 | 7 | 10 | 12 |
| | Adm FIM cog 7–10 | 7 | 9 | 8 | 9 | 8 | 11 | 11 | 14 | 12 |
| | Adm FIM cog 11–15 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 7 | 7 |
| | Adm FIM cog 16–20 | 1 | 2 | 2 | 2 | 4 | 0 | 0 | 0 | 0 |
| | Adm FIM cog ≥21 | 2 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |

Abbreviations: Adm FIM cog, admission FIM cognitive subscale; COMT, catechol-O-methyltransferase; DA, dopamine; GABA-A, gamma-aminobutyric acid-A; MAO, monoamine oxidase; NaSSA, noradrenergic and specific serotonergic antidepressant; NDRI, norepinephrine-dopamine reuptake inhibitor; NE, norepinephrine; NE-DA-5HT, norepinephrine-dopamine-5HT; NMDA, N-methyl-D-aspartate; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

* Ten patients were excluded because of missing admission FIM cognitive scores.