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## Original Article

### **Factors Associated with the Use of Laxatives in Psychiatric Emergency Wards: A Single-center University Hospital-based, Cross-sectional Study**

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## Abstract

It has been pointed out that psychotropic drugs may increase the risk of developing constipation, but there are few high-quality studies on constipation involving patients taking psychotropic drugs. In the present study, we collected data from the medical records of 1696 patients admitted to the psychiatric emergency ward of Showa University Northern Yokohama Hospital to determine the rate of laxative use in the last prescription. These patients were divided into two groups: one with and the other without laxatives. We statistically examined differences in patient background and drug therapy. The clinical dosage ratio was defined as the ratio of the dose of each drug, with the upper limit on the package insert of each drug set to 1. The results of multivariate logistic regression analysis suggested that older age, female, higher number of hospitalizations, longer length of stay, and clinical dosage ratio of conventional antidepressants, newer antidepressants, mood stabilizers, and benzodiazepines were associated with laxative

use. By individual drug category, doses of quetiapine, levomepromazine, venlafaxine, and mirtazapine may be associated with laxative use.

**Keywords:** constipation, laxatives, psychotropic drugs, side effects, psychiatric emergency ward

## Introduction

Constipation is a highly prevalent functional bowel disorder worldwide. According to the 2016 Comprehensive Survey of Living Conditions conducted by the Ministry of Health, Labour and Welfare, the prevalence of constipation in Japan was 2.5% among men and 4.6% among women, with a higher rate among women. While the proportion of women is overwhelmingly higher in the young to middle-aged population, the prevalence rate increases in both men and women after age 60. Among the elderly aged 70 or older, the proportion of men increases sharply, resulting in a decreasing sex difference.<sup>19)</sup> According to Soares, N.C. et al., the prevalence of chronic idiopathic constipation in the United States is approximately 14%, with higher rates observed among women, the elderly, and groups with a lower socioeconomic status.<sup>35)</sup> Oh, S.J. et al. conducted a large population-based cohort study of individuals with a history of constipation. They reported that 1,128 out of 4,702 subjects (24.0%) met the criteria for chronic idiopathic

constipation, and 2,246 (47.8%) were using constipation medications. Furthermore, the presence of mental disorders was associated with an increased likelihood of requiring constipation care (OR: 1.25, 95% CI: 1.09–1.44).<sup>27)</sup>

Although constipation is a universally prevalent condition, large cohort studies following more than 30,000 patients per year with functional gastrointestinal disorders have indicated that individuals with chronic constipation symptoms face a risk of reduced survival.<sup>2)</sup> Furthermore, constipation or laxative use has been shown to be independently associated with increased risks of all-cause mortality, chronic renal failure, and ischemic stroke.<sup>36)</sup> These reports indicate that constipation is a condition that influences the prognosis.

*Clinical Practice Guidelines for Chronic Constipation 2017*, compiled by the Study Group on Diagnosis and Treatment of Chronic Constipation affiliated with the Japanese Society of Gastroenterology, state that

psychotropic drugs are associated with a high risk of developing chronic constipation due to suppression of gastrointestinal tone, peristalsis, and intestinal fluid secretion mediated by anticholinergic effects. Specifically, antidepressants, certain antipsychotics, antiparkinsonian drugs (APDs), benzodiazepine (BZD) receptor agonists, and first-generation antihistamines have been noted to increase the risk of chronic constipation.<sup>26)</sup> Furthermore, the mechanism of constipation induced by antipsychotics may involve the descending pain inhibitory pathway controlling the defecation reflex. Dopamine receptor blockade suppresses the excitation of preganglionic parasympathetic nerves in the sacral spinal cord. This may reduce dopamine-mediated colonic and rectal motility via the descending pain inhibitory system, potentially causing constipation.<sup>23)</sup> Furthermore, histamine contracts intestinal smooth muscle via H1 receptors,<sup>43)</sup> suggesting that antihistamine effects may suppress intestinal contractions.

In the treatment of patients with mental disorders, various psychotropic drugs with anticholinergic, dopamine receptor-blocking, and antihistamine effects are prescribed. Furthermore, multiple categories of psychotropic drugs may be prescribed concurrently. Additionally, anticholinergic

antiparkinsonian drugs (APDs) with strong anticholinergic effects may be co-administered to treat or prevent extrapyramidal symptoms caused by antipsychotic drugs. Psychiatric patients in such treatment settings are considered to have a high risk of developing constipation. However, compared with the frequency of constipation observed in clinical practice among psychiatric patients, there are few high-quality studies examining the risk of constipation,<sup>6)</sup> and only a limited number of domestic and international guidelines related to the treatment of mental disorders mention constipation as a side effect of psychotropic drugs.<sup>10)25)</sup>

In Japan, Sato et al. conducted a questionnaire survey of 1,384 patients attending psychiatric outpatient clinics at three facilities. Defining constipation as meeting the Rome IV criteria for constipation<sup>20)</sup> or taking laxatives, the study found that 41.8% of patients met the definition of constipation used in this study. Furthermore, multivariate analysis using prescribed medication categories as explanatory variables reported that factors associated with constipation included: older age, female sex, lower BMI, presence of stress, and use of APDs, conventional antidepressants, and mood stabilizers.<sup>31)</sup>

Against this background, the authors conducted a survey on laxative use among patients admitted to psychiatric emergency wards, aiming to identify factors associated with the risk of developing constipation in psychiatric inpatients. The reason for choosing laxative use as the primary endpoint was that during hospitalization, management of physical symptoms and side effects is generally addressed, making it unlikely that constipation would be neglected, and laxative use was considered an indicator of the constipation risk.

This paper is based on content presented at the 118th Annual Meeting of the Japanese Society of Psychiatry and Neurology, with additional analysis incorporated for publication.

## **I. Background of Our Hospital and Research Methods**

Showa University Northern Yokohama Hospital (hereinafter referred to as “our hospital”) is a general hospital with 689 beds located in northern Yokohama City, Kanagawa Prefecture. It has 42 psychiatric beds on a ward eligible for psychiatric emergency hospitalization fees (super emergency ward) and 50 beds on an elderly treatment ward, serving as a core psychiatric emergency hospital for Kanagawa Prefecture. Treatment on the Super Emergency Ward is guided by

operational standards, aiming for at least 60% of patients to be discharged home within three months. When prolonged hospitalization becomes certain, patients are often transferred to other hospitals for continued treatment, as our hospital lacks wards for such transitions. Furthermore, under Kanagawa Prefecture's psychiatric emergency system, patients admitted under compulsory hospitalization or medical protective hospitalization (involuntary hospitalization with guardian's consent) at the request of the administration are, in principle, transferred to a referral hospital after completing acute-phase treatment. Consequently, the absence of long-term inpatients is a defining characteristic of our hospital.

The authors conducted a medical record review covering all patients admitted to our Super Emergency Ward between January 1, 2014, and December 31, 2021. The survey items included: age, sex, diagnoses according to ICD-10 (F0 Organic mental disorders, including symptomatic, F1 Mental and behavioral disorders due to psychoactive substance use, F2 Schizophrenia, schizotypal, and delusional disorders, F3 Mood [affective] disorders, F4 Neurotic, stress-related, and somatoform disorders, F5 Behavioral and emotional disorders associated with physiological

disturbances and physical factors, F6 Personality and behavioral disorders in adults, F7 Intellectual disability, F8 Disorders of psychological development, F9 Disorders of conduct and emotions usually beginning in childhood and adolescence, Unspecified mental disorders, G4 Intermittent and paroxysmal disorders), clinical diagnosis, duration of illness (estimated from medical records), treatment duration (number of years since initial treatment), type of admission under the Mental Health and Welfare Act, length of stay on the ward, number of hospitalizations, presence of isolation during hospitalization, use of restraints, use of electroconvulsive therapy (ECT), use of haloperidol (HPD) infusion, initial prescription upon admission (including laxatives), final prescription, and respective dosages. These items were compiled to create a database. During the study period, 217 patients were hospitalized multiple times, totaling 600 hospitalizations. However, for patients with multiple hospitalization episodes, each hospitalization was counted as one case in this study.

When examining the relationship between drug dosage and laxative use risk, dosage estimation indicators exist for certain drug categories, such as chlorpromazine, imipramine, and biperiden equivalents. However, such

indicators are absent for other drug categories, and no single dosage indicator exists that can be combined across all drugs. Furthermore, since the impact of dosage was not examined in the study by Sato et al.,<sup>31)</sup> the authors independently defined and calculated an indicator termed the “clinical dose ratio” for this study. The clinical dose ratio is a numerical value representing the ratio of the actual administered dose to maximum dose stated in the domestic package insert for each drug, with the maximum dose set as 1. While lacking significant academic merit, it is simple to calculate and was considered useful for understanding actual clinical dosing. Therefore, in this study, the clinical dose ratio was calculated for each drug, and these ratios were summed to create an indicator for the total dose by drug category and overall dose (e.g., Risperidone 6 mg =  $6/6 = 1$ , Risperidone 3 mg =  $3/6 = 0.5$ , Quetiapine (immediate-release tablets) 750 mg =  $750/750 = 1$ , Quetiapine (immediate-release tablets) 500 mg =  $500/750 = 0.67$ , Paroxetine (immediate-release tablets) 20 mg + Mirtazapine 15 mg =  $20/40 + 15/45 = 0.5 + 0.33 = 0.83$ , and Quetiapine (extended-release tablets), 300 mg =  $300/300 = 1$ ).

As statistical analysis based on the database, the laxative usage rate in the final prescription during hospitalization was initially calculated. Next, patients

prescribed laxatives were classified into the laxative-prescribed group, and those not prescribed were classified into the non-laxative group. A comparison between the two groups was performed. Continuous variables are expressed as the median (interquartile range). For significance testing, the chi-square test was used for most nominal variables, and Fisher's exact test was applied for variables with small sample sizes. The Mann-Whitney U test was applied for significance testing of continuous variables. Furthermore, to examine factors associated with laxative use, multivariate logistic regression analysis was performed with the presence of laxatives in the final prescription as the dependent variable. The following factors were initially included: age, sex (female), living alone, disability pension, public assistance, history of alcohol use, history of smoking, treatment duration, number of hospitalizations, length of stay on the ward, use of isolation, use of restraint, use of ECT, clinical dose ratio of second-generation antipsychotics (SGAs) in the final prescription, clinical dose ratio of first-generation antipsychotics (FGAs), clinical dose ratio of APDs, clinical dose ratio of newer antidepressants, clinical dose ratio of conventional antidepressants, clinical dose ratio of benzodiazepine anxiolytics, clinical dose ratio of benzodiazepines, clinical dose ratio of

mood stabilizers, clinical dose ratio of medications for attention-deficit/hyperactivity disorder (ADHD), and clinical dose ratio of anti-dementia drugs. Furthermore, based on these results, for antipsychotics, new antidepressants, and mood stabilizers, which are frequently used and exhibit significant individual differences in pharmacological effects, we compared the prescription rates and clinical dose ratios for each drug. Additionally, we separately performed multivariate logistic regression analysis using the clinical dose ratios for antipsychotics, new antidepressants, and mood stabilizers as explanatory variables. Statistical analyses were performed using Microsoft Excel 2019 and SPSS ver. 25.0.

Regarding SGA and FGA criteria, antipsychotics marketed in Japan after risperidone (1996) were defined as SGAs, while all other antipsychotics were defined as FGAs. No patients were using clozapine. Regarding APDs, amantadine was confirmed to be used by one patient in the laxative-prescribed group; all other APDs used were the following three agents with strong anticholinergic effects: biperiden, promethazine, and trihexyphenidyl. Regarding criteria for new and conventional antidepressants, drugs marketed in Japan after fluvoxamine (1999) were defined as new

antidepressants, while others were defined as conventional antidepressants. BZD-class drugs included non-BZD GABA receptor agonists. Mood stabilizers included lithium carbonate, valproic acid, carbamazepine, and lamotrigine. Quetiapine (extended-release tablets) was also included, despite the pharmacokinetics and maximum doses differing from immediate-release tablets and lacking an indication for schizophrenia. Regarding laxatives, since determining their use as needed was difficult in this study, data were compiled and analyzed for laxatives prescribed as regular medications. Laxatives used for bowel control in this study included: sennosides, senna, senna extract, magnesium oxide, mosapride citrate, pantethine, lubiprostone, elobixibat, and linaclotide. They also included Kampo medicines (Daikenchuto, Boufutsushosan, Tohakuajokito, Keishikakayakuto) confirmed from medical records to be used for bowel-control purposes.

## II. Ethical Considerations

This study was conducted based on the “Ethical Guidelines for Medical Research Involving Human Subjects” (Ministry of Health, Labour and Welfare/Ministry of Education, Culture, Sports, Science and Technology), with approval from the “Ethics Committee

for Research Involving Human Subjects at Showa University” (Receipt No. 21-160-A).

As this was an observational study based on medical records, obtaining individual consent beforehand was difficult. Therefore, the study’s purpose and implementation details were posted on Showa University’s website, ensuring that participants had the opportunity to refuse the use of their personal information. Such information was managed using anonymized identification codes, and a separate information management officer was appointed. The cross-reference table linking individuals to anonymization codes was stored on an internal hospital server isolated from external networks, with access restricted by password.

## III. Results

### 1. Subject overview

Patients admitted to our hospital’s psychiatric emergency ward between January 1, 2014, and December 31, 2021, were included. Those with multiple admission episodes at our hospital (217 patients, totaling 600 admissions) were counted as one case per admission. The total number of subjects was 1,696. The breakdown was 576 males and 1,120 females, with a median age of 49 (range: 36–64) years. The median duration of illness was 11 (range: 4–21) years, median treatment

duration was 8 (range: 2–17) years, and median number of hospitalizations was 1 (range: 1–3). Alcohol consumption history was present in 495 (29.2%), smoking history in 373 (22.0%), living alone in 217 (12.8%), disability pension receipt in 261 (15.4%), and welfare receipt in 165 (9.7%). Primary diagnoses according to ICD-10 were: F0 in 79 (4.7%), F1 in 75 (4.4%), F2 in 587 (34.6%), F3 in 581 (34.3%), F4 in 191 (11.3%), F5 in 47 (2.8%), F6 in 51 (3.0%), F7 in 30 (1.8%), F8 in 33 (1.9%), F9 in 14 (0.8%), and G4 in 5 (0.3%).

Laxatives were prescribed at the final prescription in 691 patients (40.7%), while they were not prescribed for 1,005 patients (59.3%) (Table 1).

## 2. Comparison of patient background

Continuous variables are presented as the median (interquartile range). Patients prescribed laxatives at the last prescription were classified as the laxative-prescribed group, while those without laxatives were classified as the non-laxative group. The laxative-prescribed group showed a significantly larger proportion of women ( $P < 0.001$ ). The median age was 53 (38–68) years in the laxative-prescribed group and 46 (33–59) years in the non-laxative group, indicating a significantly older age in the laxative-prescribed group ( $P < 0.001$ ). Median values for the duration of illness and treatment were 13 (5–22) and 10

(3–19) years in the laxative-prescribed group, and 9 (7–18) and 6 (4–15) years in the non-laxative group, respectively. Both were significantly longer in the laxative-prescribed group ( $P = 0.002$ ,  $P < 0.001$ ). The median number of hospitalizations was 2 (1–4) in the laxative-prescribed group and 1 (1–3) in the non-laxative group, with the laxative-prescribed group showing significantly more hospitalizations ( $P < 0.001$ ). No significant differences were observed between groups regarding alcohol consumption or smoking history. There was also no significant difference in the proportion of welfare recipients between the groups. However, the number of individuals living alone was 75 (10.9%) in the laxative-prescribed group and 142 (14.1%) in the non-laxative group, with the laxative-prescribed group showing a significantly lower rate ( $P = 0.047$ ). Disability pension recipients were significantly more common in the laxative-prescribed group (131 cases, 19.0%) compared with the non-laxative group (130 cases, 12.9%) ( $P < 0.001$ ). For primary diagnoses according to ICD-10, the laxative-prescribed group included 22 (3.2%) in F1, 42 (6.1%) in F4, and 2 (0.3%) in F8. The non-laxative group included 53 (5.3%) in F1, 149 (14.8%) in F4, and 31 (3.1%) in F8. The laxative-prescribed group showed significantly fewer cases in all these categories ( $P =$

0.039,  $P < 0.001$ ,  $P < 0.001$ ). Conversely, F3 was significantly more common in the laxative-prescribed group (299 cases, 43.3%) than in the untreated group (282 cases, 28.1%;  $P < 0.001$ ). Furthermore, when depression and bipolar disorder were analyzed separately within the F3 category, depression was significantly more common in the laxative-prescribed group ( $P < 0.001$ ), whereas no significant difference was observed between the two groups regarding bipolar disorder (Table 1).

### 3. Comparison of inpatient treatment

No significant difference was observed between groups in the rate of voluntary admission. The rate of involuntary hospitalization with guardians' consent involved 496 (71.8%) in the laxative-prescribed group and 592 (58.9%) in the laxative-untreated group, with the laxative-prescribed group showing a significantly higher rate ( $P < 0.001$ ). Conversely, for administrative involuntary hospitalization and emergency administrative involuntary hospitalization, the laxative-prescribed group included 66 (9.6%) and 6 (0.9%), respectively, while the non-laxative group included 194 (19.3%) and 36 (3.6%), respectively. The laxative-prescribed group showed significantly lower rates for both ( $P < 0.001$ ). However, no significant difference was

observed between the two groups when voluntary and involuntary admissions were combined. Isolation was performed for 227 (32.9%) in the laxative-prescribed group and 437 (43.5%) in the non-laxative group, with a significantly lower rate in the laxative-prescribed group ( $P < 0.001$ ). HPD infusion was administered to 46 (6.7%) in the laxative-prescribed group and 97 (9.7%) in the non-laxative group, with a significantly lower rate in the laxative-prescribed group ( $P = 0.029$ ). The home discharge rate involved 519 (75.1%) in the laxative-prescribed group and 658 (65.5%) in the non-laxative group, showing a significantly higher rate in the laxative-prescribed group ( $P < 0.001$ ). Regarding facility discharge, the laxative-prescribed group included 29 (4.2%) and the non-laxative group involved 19 (1.9%), with the laxative-prescribed group showing a significantly higher rate ( $P = 0.004$ ). The rate of transfer to psychiatric hospitals involved 130 (18.8%) in the laxative-prescribed group and 298 (29.7%) in the non-laxative group, with the laxative-prescribed group showing a significantly lower rate ( $P < 0.001$ ). The median length of stay was 66 (36-89) days in the laxative-prescribed group and 47 (23-83) days in the non-laxative group, with the laxative-prescribed group showing a significantly longer stay ( $P < 0.001$ ) (Table 2).

#### 4. Comparison of final prescriptions and clinical dose ratios

The overall prescription rate for psychotropic drugs, including antipsychotics, involved 678 (98.1%) in the laxative-prescribed group and 936 (93.1%) in the non-laxative group, with the laxative-prescribed group showing a significantly higher rate ( $P < 0.001$ ). For antipsychotics, no significant difference was observed between groups in overall prescription or SGA prescription rates. However, the FGA prescription rate involved 153 (22.1%) in the laxative-prescribed group and 155 (15.4%) in the non-laxative group, with the laxative-prescribed group showing a significantly higher rate ( $P < 0.001$ ). The prescription rate for APDs involved 141 (20.4%) in the laxative-prescribed group and 118 (11.7%) in the non-laxative group, with the laxative-prescribed group showing a significantly higher rate ( $P < 0.001$ ). The prescription rate for antidepressants involved 229 (33.1%) overall in the laxative-prescribed group, with 189 (27.4%) receiving new-generation antidepressants and 68 (9.8%) receiving conventional antidepressants. In contrast, the rates involved 190 (18.9%), 169 (16.8%), and 43 (4.3%), respectively, in the other group. Thus, all rates were significantly higher in the laxative-prescribed group (all  $P < 0.001$ ). For BZD-class drugs, the

laxative-prescribed group involved 385 (55.7%) overall, 192 (27.8%) for anxiolytics, and 294 (42.5%) for hypnotics. In contrast, the non-laxative group involved 472 (47.0%), 204 (20.3%), and 377 (37.5%), respectively. Therefore, the laxative-prescribed group showed significantly higher rates for all ( $P < 0.001$ ,  $P < 0.001$ ,  $P = 0.037$ ). No significant difference was observed between groups regarding the use of mood stabilizers, ADHD medications, or anti-dementia drugs (Table 3).

Clinical dose ratios are shown as the median (interquartile range). The clinical dose ratio for all psychotropic drugs, including antipsychotics, was 2.0 (1.2–2.8) in the laxative-prescribed group and 1.5 (0.7–2.3) in the non-laxative group, with the laxative-prescribed group showing a significantly higher ratio ( $P < 0.001$ ). For antipsychotics, no significant difference was observed between groups concerning overall or SGA use. However, for FGAs, the median was 0.0 (0.0–0.0) in both groups, but univariate analysis showed a significantly higher median in the laxative-prescribed group ( $P < 0.001$ ). For the clinical dose ratio of APDs, the median was 0.0 (0.0–0.0) in both groups; however, univariate analysis showed a significantly higher value in the laxative-prescribed group ( $P < 0.001$ ). For antidepressants, the overall median was 0.0 (0.0–0.5) in the laxative-

prescribed group and 0.0 (0.0–0.0) in the non-laxative group. Regarding new-generation antidepressants, the median was 0.0 (0.0–0.3) in the laxative-prescribed group and 0.0 (0.0–0.0) in the non-laxative group, with the laxative group showing significantly higher values in both cases ( $P < 0.001$ ). For conventional antidepressants, the median was 0.0 (0.0–0.0) in both groups, but univariate analysis showed that the group with laxatives had significantly higher values ( $P < 0.001$ ). The median clinical dose ratio for benzodiazepines was 0.8 (0.0–1.3) overall in the laxative-prescribed group, 0.0 (0.0–0.1) for benzodiazepine-type anxiolytics, and 0.5 (0.0–1.0) for benzodiazepine hypnotics, whereas in the non-laxative group, they were 0.5 (0.0–1.0), 0.0 (0.0–0.0), and 0.3 (0.0–1.0), respectively. The laxative-prescribed group thus showed significantly higher values for all (all  $P < 0.001$ ). No significant differences were observed between the two groups regarding mood stabilizers, ADHD medications, or anti-dementia drugs (Table 4).

##### 5. Factors associated with laxative use when drugs are classified by category

In multivariate logistic regression analysis, when the clinical dose ratio of each psychotropic drug was used as an explanatory variable by category, factors significantly correlated with

laxative use in the last prescription were: age (OR: 1.019, 95% CI: 1.012–1.026,  $P < 0.001$ ), female sex (OR: 1.351, 95% CI: 1.073–1.700,  $P = 0.011$ ), number of hospitalizations (OR: 1.068, 95% CI: 1.032–1.105,  $P < 0.001$ ), length of stay on the ward (OR: 1.005, 95% CI: 1.002–1.007,  $P < 0.001$ ), clinical dose ratio of APDs in the final prescription (OR: 5.167, 95% CI: 2.495–10.701,  $P < 0.001$ ), clinical dose ratio of new antidepressants in the final prescription (OR: 1.446, 95% CI: 1.132–1.847,  $P = 0.003$ ), clinical dose ratio of conventional antidepressants in the final prescription (OR: 6.918, 95% CI: 2.336–20.487,  $P < 0.001$ ), and clinical dose ratio of mood stabilizers in the final prescription (OR: 1.392, 95% CI: 1.032–1.876,  $P = 0.033$ ) (Table 5).

##### 6. Comparison of prescription rates by drug type in final prescriptions: antipsychotics, new antidepressants, and mood stabilizers

Prescription rates by drug type were compared for antipsychotics, newer antidepressants, and mood stabilizers. For antipsychotics, quetiapine was prescribed for 124 patients (17.9%) in the laxative-prescribed group and 140 patients (13.9%) in the non-laxative group; chlorpromazine was prescribed for 32 patients (4.6%) in the laxative-prescribed group and 23 (2.3%) in the non-laxative group. Levomepromazine

was prescribed for 106 patients (15.3%) in the group with laxatives and 103 patients (10.2%) in the group without laxatives. The prescription rates were significantly higher in the group with laxatives for all drugs ( $P = 0.025$ ,  $P = 0.007$ ,  $P = 0.002$ ). Sulpiride, however, was prescribed only in the group without laxatives (6 cases, 0.6%), with a significantly lower prescription rate in the group with laxatives ( $P = 0.041$ ) (Table 6). Among newer antidepressants, vortioxetine was prescribed for 8 patients (1.2%) in the laxative-prescribed group and 2 patients (0.2%) in the non-laxative group; duloxetine was prescribed for 38 patients (5.5%) in the laxative-prescribed group and 32 patients (3.2%) in the non-laxative group; venlafaxine was prescribed for 18 patients (2.6%) in the laxative-prescribed group and 6 patients (0.6%) in the non-laxative group. For mirtazapine, 96 patients who received it (13.9%) were in the group with laxatives and 64 (6.4%) were in the group without laxatives. The prescription rate was significantly higher in the group with laxatives for all drugs ( $P = 0.011$ ,  $P = 0.018$ ,  $P < 0.001$ ,  $P < 0.001$ ). For mood stabilizers, lamotrigine was prescribed for 67 patients (9.7%) in the laxative-prescribed group and 58 patients (5.8%) in the non-laxative group; lithium carbonate was prescribed for 59

patients (8.5%) in the laxative-prescribed group and 60 patients (6.0%) in the non-laxative group; and quetiapine (extended-release tablets) was administered to 29 patients (4.2%) in the laxative-prescribed group and 15 patients (1.5%) in the non-laxative group. The prescription rate was significantly higher in the laxative-prescribed group for all drugs ( $P = 0.002$ ,  $P = 0.041$ ,  $P < 0.001$ ) (Table 7). Furthermore, the median clinical dose ratio for all drugs was 0.0 (0.0–0.0) in both groups, showing no significant difference between them.

7. Examination of factors associated with laxative use using clinical dose ratios of antipsychotics, new antidepressants, and mood stabilizers as explanatory variables

Multivariate logistic regression analyses were performed using the clinical dose ratio of each drug (antipsychotics, new antidepressants, and mood stabilizers) as explanatory variables. The results indicated that factors significantly correlated with laxative use in the last prescription were: age (OR: 1.019, 95% CI: 1.013–1.026,  $P < 0.001$ ), sex (female) (OR: 1.356, 95% CI: 1.073–1.713,  $P = 0.011$ ), number of hospitalizations (OR: 1.063, 95% CI: 1.026–1.101,  $P = 0.001$ ), length of stay (OR: 1.004, 95% CI: 1.002–1.007,  $P = 0.001$ ), clinical dose ratio of

quetiapine in the last prescription (OR: 2.870, 95% CI: 1.333–6.179,  $P = 0.007$ ), clinical dose ratio of levomepromazine in the last prescription (OR: 3.475, 95% CI: 1.423–8.485,  $P = 0.006$ ), clinical dose ratio of APDs in the last prescription (OR: 4.333, 95% CI: 2.075–9.049,  $P < 0.001$ ), clinical dose ratio of venlafaxine in the last prescription (OR: 5.977, 95% CI: 1.657–21.561,  $P = 0.006$ ), clinical dose ratio of mirtazapine in the last prescription (OR: 2.526, 95% CI: 1.596–3.998,  $P < 0.001$ ), clinical dose ratio of conventional antidepressants in the last prescription (OR: 6.524, 95% CI: 2.207–19.284,  $P = 0.001$ ), clinical dose ratio of benzodiazepines in the last prescription (OR: 1.176, 95% CI: 1.004–1.376,  $P = 0.044$ ), and clinical dose ratio of quetiapine (extended-release) in the last prescription (OR: 5.504, 95% CI: 1.980–15.302,  $P = 0.001$ ) (Table 8).

#### IV. Discussion

In this study, the rate of laxatives in the final prescription was 40.7%, being similar to the 41.8% prevalence of constipation reported by Sato et al.<sup>31)</sup> Considering laxative use as indicative of defecation difficulties, this suggests that the prevalence of constipation among patients admitted to psychiatric emergency wards may be higher than in the general population.<sup>19)27)35)</sup>

In multivariate logistic regression analysis, factors other than medication

associated with the risk of laxative use, regardless of the explanatory variable used, were: older age, female sex, multiple hospitalizations, and longer length of hospital stay.

In the elderly, it has been reported that nerve cells within the intestinal muscle layer degenerate, the number of stellate ganglia may decrease, and the threshold for rectal sensation may increase.<sup>9)21)</sup> Additionally, in women, factors potentially influencing constipation onset include the suppression of intestinal motility by progesterone associated with menstruation, increased risk of pelvic floor muscle coordination disorders due to the number of deliveries and aging, reduced physical activity with aging, comorbidities, prescribed medications, changes in dietary intake, and changes in mental state.<sup>3)17)</sup> Horii et al. suggested that differences in neurotransmitters supplied via descending pain inhibitory pathways between sexes may influence the sex disparity in constipation incidence.<sup>12)</sup> Sato et al. also reported that being female and elderly may increase the risk of developing constipation.<sup>31)</sup> This study generated similar results. These findings suggest that, similar to the general population, both female and elderly patients among those attending psychiatric outpatient clinics and those hospitalized on psychiatric emergency

wards have a higher risk of developing constipation, with this outcome being reflected in the risk of laxative use observed in this study.

The reason for the observed association between the hospitalization frequency and prescription of laxatives remains unclear, but schizophrenia is known to potentially reduce treatment responsiveness through repeated relapses.<sup>29)39)42)</sup> Therefore, when schizophrenia patients experience repeated hospitalizations due to relapse, their treatment responsiveness to antipsychotics may decrease. This could lead to further increases in antipsychotic dosage or the addition of antipsychotic agents, potentially increasing the need for laxative administration. Furthermore, although not shown in this paper, comparing the overall groups with and without prescribed laxatives revealed no significant difference in the rate of bipolar disorder. However, in patients with this disorder, the laxative-prescribed group showed significantly more hospitalizations in univariate analysis. Regarding bipolar disorder, reports suggest that patients with multiple episodes have a reduced cerebral cortex volume compared with those experiencing their first episode, indicating a progressive disease.<sup>1)</sup> This suggests that, similar to schizophrenia, repeated relapses may reduce

treatment responsiveness, necessitate higher doses of psychotropic medications, and consequently increase the risk of laxative use, potentially influencing the overall association with the number of hospitalizations. For other disorders, no evidence linking hospitalization frequency with psychotropic drug dosage or laxative-prescribed risk was found. However, regardless of the disorder, multifaceted future investigation is warranted regarding the potential for patients experiencing repeated relapses or recurrences to become treatment-resistant, leading to increased prescriptions, or for clinicians to increase psychotropic drug dosages due to the desire to prevent relapse.

Regarding the association between length of hospital stay and laxative use, the impact of reduced physical activity due to hospitalization is a possible factor. The link between physical inactivity and constipation is also noted in *Clinical Practice Guidelines for Chronic Constipation 2017*.<sup>26)</sup> Kaganoi et al. reported that while the average daily energy expenditure for healthy individuals was 350.9 kilocalories, it was only 42 kilocalories for patients hospitalized on psychiatric wards.<sup>15)</sup> Furthermore, the relationship with stress may also need to be considered. Stress is thought to promote a sympathetic nervous system dominance,

which can reduce intestinal peristalsis and inhibit intestinal fluid secretion, thereby increasing the likelihood of constipation.<sup>7)</sup> Sato et al. reported that the presence of stress was also associated with constipation risk in outpatients.<sup>31)</sup> Super emergency wards predominantly admit involuntary patients, and some may require physical restraint due to factors such as significant psychomotor agitation or high risk of attempted suicide. Involuntary hospitalization is associated with stigma, negatively impacting QOL and self-esteem. When comparing involuntary medication, mechanical restraint, and combined measures, mechanical restraint and combined measures have been reported to cause even higher stress than involuntary medication.<sup>8)30)</sup> Therefore, involuntary hospitalization and compulsory treatment without consent are considered to load marked stress on patients. Consequently, on psychiatric emergency wards, prolonged hospitalization may increase the risk of laxative use due to the combined effects of physical inactivity and stress. Future studies should also examine the association between prolonged involuntary hospitalization and physical symptoms. Furthermore, the laxative-prescribed group included significantly less patients admitted for compulsory treatment, who most

require such intervention. However, since patients requiring compulsory admission often present as first-episode cases or show interrupted medical care, and many begin oral medication for the first time at our hospital, the overall dosage of psychotropic drugs tends to be low. In addition, due to Kanagawa's emergency system, patients are usually transferred to other hospitals within an average of 14 days, making prolonged non-voluntary admission relatively rare. Therefore, it is considered that the risk of laxative use was relatively low.

Regarding medications, when the category-specific clinical dose ratios of psychotropic drugs were used as explanatory variables, the clinical dose ratios at the last prescription of antiparkinsonian drugs, newer antidepressants, conventional antidepressants, and mood stabilizers were significantly correlated with the laxative-prescribed group. These findings suggest that higher doses of medications belonging to these categories may increase the risk of laxative use.

Regarding antipsychotics, similar to the report by Sato et al., when multivariate analysis was performed encompassing SGAs and FGAs respectively, no association was identified between antipsychotic use and the risk of laxative administration.<sup>31)</sup> Concerning this point,

as Sato et al. discussed, the inclusion of both SGAs and FGAs may have resulted in the effects of drugs with strong dopamine receptor blocking and anticholinergic actions being offset by those with weaker effects, potentially reducing the observed association.<sup>31)</sup> Furthermore, Sato et al.'s study involved outpatients, whereas this study focused on inpatients on psychiatric emergency wards. Consequently, neither study included clozapine users, who reportedly exhibit a high incidence of constipation,<sup>13)</sup> and both incorporated very few long-term inpatients. These patient population biases may also have contributed to the findings. Previous studies pointed out that constipation caused by antipsychotics may lead to severe physical complications and premature death.<sup>4)5)</sup> According to Talley, N.J. et al., the risk of developing constipation among antipsychotic users was reportedly 1.9 times higher.<sup>40)</sup> Considering these points, the results of this study, which diverge from previous research, were considered to be influenced by significant differences in pharmacological effects among antipsychotics. Therefore, reanalysis was performed using the clinical dose ratio of each drug as an explanatory variable. The results showed that quetiapine, levomepromazine, and quetiapine (extended-release tablets),

classified as a mood stabilizer, were associated with the clinical dose ratio. Quetiapine has relatively stronger anticholinergic effects than dopamine D2 blocking effects and also exhibits strong antihistamine effects.<sup>32)</sup> It was considered that these combined actions could increase the risk of laxative use. A meta-analysis by Suttajit, S. et al. on the efficacy of quetiapine for acute depressive episodes in bipolar disorder patients also reported significantly higher risks of constipation and dry mouth.<sup>37)</sup> Levomepromazine also possesses anticholinergic and antihistamine effects, suggesting that it could contribute to constipation through a similar mechanism. Furthermore, Inagaki et al. analyzed the incidence rates of adverse events in clinical trials and post-marketing surveillance of antipsychotics. The incidence rates of constipation were: 23.66–33.8% for clozapine, 14.4% for haloperidol, and 4.71–15.45% for olanzapine, risperidone, blonanserin, paliperidone, perospirone, quetiapine, and aripiprazole; for asenapine, brexpiprazole, and lurasidone, they were 1.8–3.2%.<sup>13)</sup> Furthermore, Lin, C.H. et al. found that among patients discharged in Taiwan between 2006 and 2017 who were prescribed a single SGA ( $n = 11,861$ ), 3,336 (28.1%) were concurrently using laxatives. Advanced age and high-dose antipsychotic and anticholinergic

medication use were associated with an increased rate of laxative use. Among SGAs, clozapine was associated with the highest laxative-prescribed rate, followed by zotepine, quetiapine, and olanzapine. Risperidone, amisulpride, aripiprazole, paliperidone, and ziprasidone showed similar laxative-prescribed rates.<sup>22)</sup> These findings suggest that antipsychotics, despite significant differences in pharmacologic effects and the types and frequencies of side effects depending on the drug, may independently increase the risk of constipation. Therefore, caution is warranted even for antipsychotics that showed no significant correlation in this study, as well as for chlorpromazine, which showed a significant difference based on univariate analysis.

Regarding antiparkinsonian drugs, all medications confirmed as used in this study, except for one case of amantadine, were agents that alleviate Parkinsonian symptoms via anticholinergic effects. Therefore, as expected, anticholinergic effects were considered to increase the risk of laxative use.

Regarding antidepressants, an online survey on side effects found that 73.4% of respondents experienced side effects, with the most common being drowsiness, fatigue, stomach discomfort, constipation, dizziness, dry mouth, and weight loss. Even newer

antidepressants, considered to have fewer side effects and relatively weaker anticholinergic effects than classical antidepressants like tricyclics and tetracyclics, showed that the incidence of gastrointestinal symptoms (nausea/vomiting, diarrhea, constipation, abdominal pain, indigestion, loss of appetite, dry mouth, etc.) within 12 weeks after treatment initiation was higher for all antidepressants than a placebo.<sup>28)</sup> Furthermore, studies examining the improvement of psychiatric symptoms, side effects, and treatment response rates when antidepressants were added to antipsychotics in schizophrenia treatment reported that the group receiving antidepressants in addition to antipsychotics included a higher number of patients complaining of abdominal pain, constipation, dizziness, and dry mouth<sup>11)</sup>; these conditions were reported more frequently in the group receiving antidepressants in addition to antipsychotics. In this study, as expected, a correlation was observed between the clinical dose ratio of conventional antidepressants, which generally exhibit strong anticholinergic and antihistamine effects, and the risk of laxative use. However, in multivariate analysis using the clinical dose ratio of each new-generation antidepressant with distinct pharmacological actions as an

explanatory variable, the clinical dose ratios of venlafaxine and mirtazapine were significantly correlated with laxative use. Venlafaxine has been reported to exhibit more frequent side effects of dry mouth and constipation compared with citalopram, a selective serotonin reuptake inhibitor (SSRI).<sup>33)</sup> However, regarding mirtazapine, Watanabe, N. et al. reported that the risk of constipation was relatively low.<sup>41)</sup> The CANMAT guidelines report constipation incidence rates of 15% for venlafaxine immediate-release tablets, 8% for extended-release tablets, and 13% for mirtazapine.<sup>16)</sup> Furthermore, for vortioxetine and duloxetine, which showed significant differences in univariate analysis, the same guidelines report constipation incidence rates of 4 and 11%, respectively, being lower than those for the SSRIs fluvoxamine and paroxetine.<sup>16)</sup> Notably, vortioxetine has been reported to be associated with a low incidence of constipation during clinical trials.<sup>38)</sup> Given these findings, it is currently difficult to provide a clear pharmacological or statistical explanation for the results of this study. However, it is considered necessary to note that there are differences in the incidence of constipation among newer antidepressants, and constipation may occur with certain agents. Nevertheless, the results of this study require

cautious interpretation. For drugs with evidence from a small number of cases, further investigation is warranted to determine whether the observed association could result from their use specifically to avoid constipation. Thus, further detailed investigation is considered necessary.

Regarding benzodiazepine (BZD) drugs, in the univariate analysis of clinical dose ratios, the clinical dose ratios for all BZD drugs, anxiolytics, and hypnotics were significantly higher in the laxative-prescribed group. In the multivariate analysis, the clinical dose ratio of BZD hypnotics was associated with the risk of laxative use. BZD drugs also possess anticholinergic effects and are associated with a risk of constipation, as pointed out in *Clinical Practice Guidelines for Chronic Constipation 2017*.<sup>26)</sup> A systematic review examining the efficacy of long-term BZD use for anxiety disorders, based on 8 RCTs ( $n = 1,228$ ), reported that BZDs were associated with a higher incidence of constipation and dry mouth compared with placebo use.<sup>34)</sup> Therefore, it is considered necessary to be mindful that benzodiazepine drugs may promote the onset of constipation via their anticholinergic effects. Concerning mood stabilizers, univariate analysis showed significantly higher prescription rates for lamotrigine, lithium carbonate, and quetiapine

(extended-release tablets) in the laxative-prescribed group. However, multivariate analysis revealed only that the clinical dose ratio of quetiapine (extended-release tablets) was significantly correlated, with no association found for the clinical dose ratios of other mood stabilizers. These results suggest that when mood stabilizers are analyzed collectively, quetiapine (extended-release tablets) may have a relatively greater impact. However, a cross-sectional study on gastrointestinal disorders associated with antiepileptic drugs (including monotherapy and combination therapy) reported the following frequencies: heartburn 34.6%, nausea 33.7%, constipation 26.0%, vomiting 22.1%, diarrhea 21.2%, and dysphagia 19.2%.<sup>14)</sup> Furthermore, case reports exist of refractory constipation developing after lithium carbonate administration.<sup>24)</sup> Therefore, caution regarding the occurrence of constipation is also warranted for mood stabilizers other than quetiapine (extended-release tablets). Regardless, as this was a cross-sectional study based on real-world clinical data, variability exists in the prescription frequency and dosage of psychotropic drugs. For medications with low prescription frequencies or dosages, statistical errors may be more likely to occur, and detecting associations might be difficult.

Therefore, the associations observed for each medication in this study should only be interpreted as indicative at this stage.

Furthermore, in this study, to account for potential multicollinearity between diagnoses and prescribed medications, and clarify the effects of psychotropic drugs, diagnoses were not included in the multivariate analysis, and only univariate analyses by ICD-10-based categories were performed. Although not shown in this paper, when examined by diagnosis, patients in the non-laxative group within the F1 category had significantly shorter length of stay and lower home discharge rates compared with patients in the same category who received laxatives, while also showing the largest proportion of administrative involuntary hospitalizations. Many involuntarily admitted patients received initial treatment through Kanagawa Prefecture's psychiatric emergency system and were transferred once a certain level of stability had been achieved. Consequently, their hospitalization period at our hospital was short, resulting in lower final prescription volumes and fewer laxative prescriptions. The larger proportion of such patients likely contributed to the higher ratio of the non-laxative group in F1. In F2, no significant difference was observed in the ratio of laxative-

prescribed versus non-laxative groups. The laxative-prescribed group in F2 showed an older age, longer disease and treatment durations, and a greater number of hospitalizations. Regarding psychotropic drugs, while no significant difference was observed in the clinical dose ratio of antipsychotics, the usage rate and clinical dose ratio of antidepressants, APDs, and benzodiazepines were significantly higher. Therefore, in this study, laxative use among patients in the F2 category was considered to reflect not only the patient background but also the quantity and type of psychotropic medications. In the F3 category, the proportion of the laxative-prescribed group was significantly larger overall. However, no significant difference was observed in bipolar disorder, while a significant difference was found in depression, suggesting a greater influence of antidepressants. In the F4 category, the clinical dose ratio of psychotropic drugs in the laxative-prescribed group tended to be higher compared with the non-laxative group in the same category ( $P = 0.08$ ). Although the non-laxative group was more common overall in F4, it was considered that laxative prescriptions were necessary for a small number of patients receiving higher doses. Patients in category F8 had a lower overall need for drug therapy and lower

prescription volumes, suggesting a reduced need for laxatives. Thus, even when examined by diagnosis, the influence of psychotropic drugs was considered significant. However, further investigation may be necessary, such as studies targeting patients not taking oral medications, to assess the impact of the disease itself.

Regarding the clinical dose ratio used as a dosage indicator in this study, it was considered advantageous for its simplicity of calculation and applicability to any drug with an upper limit specified in its package insert. Furthermore, the odds ratio used in multivariate analysis generally reflects the association when using up to the maximum dose of a single agent, making dosage visualization easier. Additionally, it was considered useful because it can be applied to drugs lacking established conversion values, such as the imipramine equivalent for antidepressants and diazepam equivalent for benzodiazepines. However, the clinical dose ratio is not an indicator defined based on pharmacological effects. Considering its divergence from the aforementioned conversion values, and the fact that the action characteristics, metabolic pathways, and individual variations in metabolism are not necessarily identical for each drug, its significance should be viewed as limited to this study.

It was used as a calculation method solely for the purpose of examining dose-dependent associations, and should be considered merely as a reference in an academic context.

This study shares many similarities with the report by Sato et al.<sup>31)</sup> Together with this study, factors such as: age, sex (female), APDs, newer antidepressants, conventional antidepressants, and mood stabilizers, which were commonly identified in two studies targeting different populations, were considered to be associated with the risks of constipation and laxative use. Although interpretation of the results warrants further consideration, psychotropic drugs were again confirmed to potentially increase the risk of developing constipation overall. For the drugs identified in this study, a dose-dependent increase in risk was suggested. When treating mental disorder patients, pharmacotherapy should be selected with regard to the life prognosis. As one strategy, it is necessary to consider pharmacotherapy that is less likely to cause constipation.

## V. Limitations of the Study

Limitations of this study included: being a single-center investigation; being a cross-sectional study, thus unable to demonstrate causation; the potential for bias due to counting each hospitalization episode as one case for

patients with multiple admission episodes at our hospital; the fact that laxative use does not necessarily equate to constipation; the impact of the underlying disease itself was not examined, the effect of duration of use was not assessed, the use of laxatives on an as-needed basis was not considered, other comorbid conditions were not evaluated, the clinical dose ratio used as a dosage indicator is a proprietary metric, the analysis encompassing multiple psychotropic drugs may have resulted in pharmacological effects being offset within categories, the number of cases varied significantly in the drug-specific analyses, the clinical dose ratio requires further evaluation regarding its validity as a dosage indicator, and the study's focus on psychiatric emergency ward inpatients limits its generalizability to the entire psychiatric inpatient population.

## Conclusion

The results of this study indicate that the rate of laxative use among inpatients on our psychiatric emergency ward exceeds 40%. Advanced age, female sex, multiple hospitalizations, and longer length of stay on the ward were shown to increase the risk of laxative use. Furthermore, when medications were examined comprehensively by category, the dosage of antiparkinsonian drugs

(APDs), conventional antidepressants, new antidepressants, and mood stabilizers was associated with the risk of laxative use. In multivariate analysis using antipsychotics, new antidepressants, and mood stabilizers as individual explanatory variables, significant correlations were observed for several drugs, including benzodiazepines, as well as several antipsychotics that had shown no significant differences in the category-specific analysis. Associations should be interpreted with caution because the differences in case numbers were large in the drug-specific analysis, it was considered that reducing the dosage or avoiding administration of these drugs might lower the risk of laxative use. Further studies with larger case numbers are needed.

There are no conflicts of interest to disclose regarding this paper.

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表1 患者背景の比較

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
性別 男	576 (34.0%)	199 (28.8%)	377 (37.5%)	<0.001***
女	1,120 (66.0%)	492 (71.2%)	628 (62.5%)	
年齢 (歳)	49 (36~64)	53 (38~68)	46 (33~59)	<0.001***
罹病期間 (年)	11 (4~21)	13 (5~22)	9 (7~18)	0.002**
治療期間 (年)	8 (2~17)	10 (3~19)	6 (4~15)	<0.001***
入院回数 (回)	1 (1~3)	2 (1~4)	1 (1~3)	<0.001***
飲酒歴	495 (29.2%)	194 (28.1%)	301 (30.0%)	N. S.
喫煙歴	373 (22.0%)	143 (20.7%)	230 (22.9%)	N. S.
单身生活	217 (12.8%)	75 (10.9%)	142 (14.1%)	0.047*
障害年金	261 (15.4%)	131 (19.0%)	130 (12.9%)	<0.001***
生活保護	165 (9.7%)	71 (10.3%)	94 (9.4%)	N. S.
ICD-10 F0	79 (4.7%)	33 (4.8%)	46 (4.6%)	N. S.
F1	75 (4.4%)	22 (3.2%)	53 (5.3%)	0.039*
F2	587 (34.6%)	235 (34.0%)	352 (35.0%)	N. S.
F3	581 (34.3%)	299 (43.3%)	282 (28.1%)	<0.001***
双極性障害	250 (14.7%)	104 (15.1%)	146 (14.5%)	N. S.
うつ病	216 (12.7%)	125 (18.1%)	91 (9.1%)	<0.001***
F4	191 (11.3%)	42 (6.1%)	149 (14.8%)	<0.001***
F5	47 (2.8%)	21 (3.0%)	26 (2.6%)	N. S.
F6	51 (3.0%)	17 (2.5%)	34 (3.4%)	N. S.
F7	30 (1.8%)	13 (1.9%)	17 (1.7%)	N. S.
F8	33 (1.9%)	2 (0.3%)	31 (3.1%)	<0.001***
F9	14 (0.8%)	5 (0.7%)	9 (0.9%)	N. S.
G4	5 (0.3%)	2 (0.3%)	3 (0.3%)	N. S.

連続変数の表記は中央値 (四分位範囲) で示した。平均 (標準偏差) \* <0.05, \*\* <0.01, \*\*\* <0.001

緩下剤あり群・緩下剤なし群の比較において、名義変数には $\chi^2$ 検定、連続変数には Mann-Whitney のU検定を用いた。

Table 1: Comparison of patient background

Total (n = 1,696)

Laxative-prescribed group (n = 691)

Non-laxative group (n = 1,005)

P

Sex

Male	576 (34.0%)	199 (28.8%)	377 (37.5%)	<0.001***
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Female	1,120 (66.0%)	492 (71.2%)	628 (62.5%)	
Age (years)				
	49 (36–64)	53 (38–68)	46 (33–59)	<0.001***
Duration of illness (years)				
	11 (4–21)	13 (5–22)	9 (7–18)	0.002**
Treatment duration (years)				
	8 (2–17)	10 (3–19)	6 (4–15)	<0.001***
Number of hospitalizations (times)				
	1 (1–3)	2 (1–4)	1 (1–3)	<0.001***
History of alcohol consumption				
	495 (29.2%)	194 (28.1%)	301 (30.0%)	N.S.
History of smoking				
	373 (22.0%)	143 (20.7%)	230 (22.9%)	N.S.
Living alone				
	217 (12.8%)	75 (10.9%)	142 (14.1%)	0.047*
Disability pension				
	261 (15.4%)	131 (19.0%)	130 (12.9%)	<0.001***
Public assistance				
	165 (9.7%)	71 (10.3%)	94 (9.4%)	N.S.
ICD—10				
F0	79 (4.7%)	33 (4.8%)	46 (4.6%)	N.S.
F1	75 (4.4%)	22 (3.2%)	53 (5.3%)	0.039*
F2	587 (34.6%)	235 (34.0%)	352 (35.0%)	N.S.
F3	581 (34.3%)	299 (43.3%)	282 (28.1%)	<0.001***
Bipolar disorder	250 (14.7%)	104 (15.1%)	146 (14.5%)	N.S.
Depression	216 (12.7%)	125 (18.1%)	91 (9.1%)	<0.001***
F4	191 (11.3%)	42 (6.1%)	149 (14.8%)	<0.001***
F5	47 (2.8%)	21 (3.0%)	26 (2.6%)	N.S.
F6	51 (3.0%)	17 (2.5%)	34 (3.4%)	N.S.
F7	30 (1.8%)	13 (1.9%)	17 (1.7%)	N.S.
F8	33 (1.9%)	2 (0.3%)	31 (3.1%)	<0.001***
F9	14 (0.8%)	5 (0.7%)	9 (0.9%)	N.S.
G4	5 (0.3%)	2 (0.3%)	3 (0.3%)	N.S.

Continuous variables are expressed as median (interquartile range). Mean (standard deviation) \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

For comparisons between the laxative-treated and laxative-untreated groups, the  $\chi^2$  test was used for nominal variables and Mann–Whitney U test for continuous variables.

表 2 入院治療の比較

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
入院形態 任意	305 (18.0%)	123 (17.8%)	182 (18.1%)	N. S.
医療保護措置	1,088 (64.2%)	496 (71.8%)	592 (58.9%)	<0.001***
緊急措置	260 (15.3%)	66 ( 9.6%)	194 (19.3%)	<0.001***
応急	42 ( 2.5%)	6 ( 0.9%)	36 ( 3.6%)	<0.001***
鑑定入院	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	—
	1 ( 0.1%)	0 ( 0.0%)	1 ( 0.1%)	N. S.
隔離施行	664 (39.2%)	227 (32.9%)	437 (43.5%)	<0.001***
拘束施行	488 (28.8%)	183 (26.5%)	305 (30.3%)	N. S.
HPD 点滴施行	143 ( 8.4%)	46 ( 6.7%)	97 ( 9.7%)	0.029*
ECT 施行	337 (19.9%)	174 (25.2%)	163 (16.2%)	<0.001***
自宅退院	1,177 (69.4%)	519 (75.1%)	658 (65.5%)	<0.001***
施設退院	49 ( 2.9%)	29 ( 4.2%)	20 ( 2.0%)	0.04*
転棟	19 ( 1.1%)	5 ( 0.7%)	14 ( 1.4%)	N. S.
転院 (精神)	428 (25.2%)	130 (18.8%)	298 (29.7%)	<0.001***
転院 (身体)	19 ( 1.1%)	7 ( 1.0%)	12 ( 1.2%)	N. S.
死亡	4 ( 0.2%)	1 ( 0.1%)	3 ( 0.3%)	N. S.
在棟日数	57 (26~87)	66 (36~89)	47 (23~83)	<0.001***

連続変数の表記は中央値 (四分位範囲) で示した。\* <0.05, \*\* <0.01, \*\*\* <0.001  
緩下剤あり群・緩下剤なし群の比較において、名義変数には  $\chi^2$  検定、連続変数には Mann–Whitney の U 検定を用いた。死亡の比較については Fisher の正確確率検定を用いた。

Table 2: Comparison of inpatient treatment

Total (n=1,696)

Laxative-prescribed group (n=691)

Non-laxative group (n=1,005)

P

Type of admission

Voluntary

305 (18.0%) 123 (17.8%) 182 (18.1%) N.S.

Involuntary with guardians' consent

	1,088 (64.2%)	496 (71.8%)	592 (58.9%)	<0.001***
Administrative involuntary				
	260 (15.3%)	66 (9.6%)	194 (19.3%)	<0.001**
Emergency administrative involuntary				
	42 (2.5%)	6 (0.9%)	36 (3.6%)	<0.001***
First aid				
	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
Forensic admission				
	1 (0.1%)	0 (0.0%)	1 (0.1%)	N.S.
Isolation implemented				
	664 (39.2%)	227 (32.9%)	437(43.5%)	<0.001***
Restraint implemented				
	488 (28.8%)	183 (26.5%)	305 (30.3%)	N.S.
HPD infusion implementation				
	143 (8.4%)	46 (6.7%)	97 (9.7%)	0.029*
ECT performed				
	337 (19.9%)	174 (25.2%)	163 (16.2%)	<0.001***
Discharge to home				
	1,177 (69.4%)	519 (75.1%)	658 (65.5%)	<0.001***
Facility discharge				
	49 (2.9%)	29 (4.2%)	20 (2.0%)	0.04*
Transfer to another ward				
	19 (1.1%)	5 (0.7%)	14 (1.4%)	N.S.
Transfer to another hospital (psychiatric)				
	428 (25.2%)	130 (18.8%)	298 (29.7%)	<0.001***
Transfer to another hospital (non-psychiatric)				
	19 (1.1%)	7 (1.0%)	12 (1.2%)	N.S.
Death				
	4 (0.2%)	1 (0.1%)	3 (0.3%)	N.S.
Length of stay				
	57 (26–87)	66 (36–89)	47 (23–83)	<0.001***

Continuous variables are expressed as median (interquartile range). \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

For comparisons between the laxative-prescribed and non-laxative groups, the chi-square test was used for nominal variables and Mann–Whitney U test for continuous

variables. Fisher's exact test was used for comparing mortality rates.

表3 最終処方・処方率の比較

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
向精神薬使用	1,614 (95.2%)	678 (98.1%)	936 (93.1%)	<0.001**
抗精神病薬使用	1,294 (76.3%)	534 (77.3%)	760 (75.6%)	N. S.
SGA 使用	1,199 (70.7%)	495 (71.6%)	704 (70.0%)	N. S.
FGA 使用	308 (18.2%)	153 (22.1%)	155 (15.4%)	<0.001**
抗バ薬使用	259 (15.3%)	141 (20.4%)	118 (11.7%)	<0.001**
抗うつ薬使用	419 (24.7%)	229 (33.1%)	190 (18.9%)	<0.001**
新規抗うつ薬使用	358 (21.1%)	189 (27.4%)	169 (16.8%)	<0.001**
従来型抗うつ薬使用	111 ( 6.5%)	68 ( 9.8%)	43 ( 4.3%)	<0.001**
BZD 系薬剤使用	857 (50.5%)	385 (55.7%)	472 (47.0%)	<0.001**
BZD 系抗不安薬使用	396 (23.3%)	192 (27.8%)	204 (20.3%)	<0.001**
BZD 系睡眠薬使用	671 (39.6%)	294 (42.5%)	377 (37.5%)	0.037*
気分安定薬使用	672 (39.6%)	288 (41.7%)	384 (38.2%)	N. S.
ADHD 治療薬使用	10 ( 0.6%)	6 ( 0.9%)	4 ( 0.4%)	N. S.
抗認知症薬使用	15 ( 0.9%)	9 ( 1.3%)	6 ( 0.6%)	N. S.

\* <0.05, \*\* <0.001

緩下剤あり群・緩下剤なし群の比較において、 $\chi^2$  検定を用いた。ADHD 治療薬、抗認知症薬の比較については Fisher の正確確率検定を用いた。

Table 3: Comparison of final prescriptions and prescription rates

Total (n=1,696)

Laxative-prescribed group (n=691)

Non-laxative group (n=1,005)

P

Psychotropic drug use

1,614 (95.2%) 678 (98.1%) 936 (93.1%) <0.001\*\*

Antipsychotic drug use

1,294 (76.3%) 534 (77.3%) 760 (75.6%) N.S.

SGA use

1,199 (70.7%) 495 (71.6%) 704 (70.0%) N.S.

FGA use

308 (18.2%) 153 (22.1%) 155 (15.4%) <0.001\*\*

APD use

	259 (15.3%)	141 (20.4%)	118 (11.7%)	<0.001**
Antidepressant use				
	419 (24.7%)	229 (33.1%)	190 (18.9%)	<0.001**
New antidepressant use				
	358 (21.1%)	189 (27.4%)	169 (16.8%)	<0.001**
Conventional antidepressant use				
	111 (6.5%)	68 (9.8%)	43 (4.3%)	<0.001**
Benzodiazepine use				
	857 (50.5%)	385 (55.7%)	472 (47.0%)	<0.001**
Benzodiazepine anxiolytic use				
	396 (23.3%)	192 (27.8%)	204 (20.3%)	<0.001**
Benzodiazepine hypnotic use				
	671 (39.6%)	294 (42.5%)	377 (37.5%)	0.037*
Mood stabilizer use				
	672 (39.6%)	288 (41.7%)	384 (38.2%)	N. S.
ADHD drug use				
	10 (0.6%)	6 (0.9%)	4 (0.4%)	N. S.
Antidementia drug use				
	15 (0.9%)	9 (1.3%)	6 (0.6%)	N. S.

\*<0.05, \*\*<0.001

The  $\chi^2$  test was used for comparisons between the laxative-prescribed and non-laxative groups. Fisher's exact probability test was used for comparisons of ADHD medications and anti-dementia drugs.

表 4 最終処方・臨床用量比の比較

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
向精神薬臨床用量比 (抗パ薬含む)	1.7 (1.0~2.5)	2.0 (1.2~2.8)	1.5 (0.7~2.3)	<0.001*
抗精神病薬臨床用量比	0.3 (0.0~0.9)	0.3 (0.0~1.0)	0.3 (0.0~0.8)	N. S.
SGA 臨床用量比	0.3 (0.0~0.8)	0.3 (0.0~0.8)	0.3 (0.0~0.8)	N. S.
FGA 臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	<0.001*
抗パ薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	<0.001*
抗うつ薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.5)	0.0 (0.0~0.0)	<0.001*
新規抗うつ薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.3)	0.0 (0.0~0.0)	<0.001*
従来型抗うつ薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	<0.001*
BZD系薬剤臨床用量比	0.5 (0.0~1.0)	0.8 (0.0~1.3)	0.5 (0.0~1.0)	<0.001*
BZD系抗不安薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.1)	0.0 (0.0~0.0)	<0.001*
BZD系睡眠薬臨床用量比	0.5 (0.0~1.0)	0.5 (0.0~1.0)	0.3 (0.0~1.0)	<0.001*
気分安定薬臨床用量比	0.0 (0.0~0.4)	0.0 (0.0~0.5)	0.0 (0.0~0.3)	N. S.
ADHD治療薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	N. S.
抗認知症薬臨床用量比	0.0 (0.0~0.0)	0.0 (0.0~0.0)	0.0 (0.0~0.0)	N. S.

臨床用量比の表記は中央値（四分位範囲）で示した。\* <0.001

緩下剤あり群・緩下剤なし群の比較において、Mann-WhitneyのU検定を用いた。

Table 4: Comparison of final prescription and clinical dose ratios

Total (n=1,696)

Laxative-prescribed group (n=691)

Non-laxative group (n=1,005)

P

Psychotropic drug clinical dose ratio (including APDs)

1.7 (1.0–2.5)    2.0 (1.2–2.8)    1.5 (0.7–2.3)    <0.001\*

Clinical dose ratio of antipsychotics

0.3 (0.0–0.9)    0.3 (0.0–1.0)    0.3 (0.0–0.8)    N. S.

Clinical dose ratio of SGA

0.3 (0.0–0.8)    0.3 (0.0–0.8)    0.3 (0.0–0.8)    N. S.

Clinical dose ratio of FGA

0.0 (0.0–0.0)    0.0 (0.0–0.0)    0.0 (0.0–0.0)    <0.001\*

Clinical dose ratio of APDs

0.0 (0.0–0.0)    0.0 (0.0–0.0)    0.0 (0.0–0.0)    <0.001\*

Clinical dose ratio of antidepressants

0.0 (0.0–0.0)    0.0 (0.0–0.5)    0.0 (0.0–0.0)    <0.001\*

Clinical dose ratio of new antidepressants	0.0 (0.0–0.0)	0.0 (0.0–0.3)	0.0 (0.0–0.0)	<0.001*
Clinical dose ratio of conventional antidepressants	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	<0.001*
Clinical dose ratio of benzodiazepines	0.5 (0.0–1.0)	0.8 (0.0–1.3)	0.5 (0.0–1.0)	<0.001*
Clinical dose ratio of benzodiazepine anxiolytics	0.0 (0.0–0.0)	0.0 (0.0–0.1)	0.0 (0.0–0.0)	<0.001*
Clinical dose ratio of benzodiazepine hypnotics	0.5 (0.0–1.0)	0.5 (0.0–1.0)	0.3 (0.0–1.0)	<0.001*
Clinical dose ratio of mood stabilizers	0.0 (0.0–0.4)	0.0 (0.0–0.5)	0.0 (0.0–0.3)	N. S.
Clinical dose ratio of ADHD treatment drugs	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	N. S.
Clinical dose ratio of anti-dementia drugs	0.0 (0.0–0.0)	0.0 (0.0–0.0)	0.0 (0.0–0.0)	N. S.

Clinical dose ratios are expressed as median (interquartile range). \*<0.001

The Mann–Whitney U test was used to compare the laxative-prescribed and non-laxative groups.

表5 最終処方・緩下剤投与ありに関連する因子（薬剤についてカテゴリー別の臨床用量比を説明変数としたもの）

変数	B	S. E.	Wald	VIF	Odds ratio	95% CI		P
						下限	上限	
年齢 <sup>a</sup>	0.019	0.003	33.104	1.261	1.019	1.012	1.026	<0.001***
性別（女性） <sup>b</sup>	0.301	0.117	6.545	1.082	1.351	1.073	1.700	0.011*
入院回数 <sup>c</sup>	0.065	0.017	14.152	1.354	1.068	1.032	1.105	<0.001***
在棟日数 <sup>d</sup>	0.005	0.001	13.109	1.139	1.005	1.002	1.007	<0.001***
最終抗パ薬 臨床用量比 <sup>e</sup>	1.642	0.371	19.543	1.124	5.167	2.495	10.701	<0.001***
最終新規抗うつ薬 臨床用量比 <sup>e</sup>	0.369	0.125	8.731	1.208	1.446	1.132	1.847	0.003**
最終従来型抗うつ薬 臨床用量比 <sup>e</sup>	1.934	0.554	12.193	1.026	6.918	2.336	20.487	<0.001**
最終気分安定薬 臨床用量比 <sup>e</sup>	0.330	0.153	4.691	1.094	1.392	1.032	1.876	0.033*

変数増加法による。\* <0.05, \*\* <0.01, \*\*\* <0.001

目的変数：最終処方での緩下剤使用あり

説明変数：年齢，性別（女性），単身生活，障害年金，生活保護，飲酒歴，喫煙歴，治療期間，入院回数，在棟日数，隔離施行，拘束施行，ECT 施行，最終 SGA 臨床用量比，最終 FGA 臨床用量比，最終抗パ薬臨床用量比，最終新規抗うつ薬臨床用量比，最終従来型抗うつ薬臨床用量比，最終 BZD 系抗不安薬臨床用量比，最終 BZD 系睡眠薬臨床用量比，最終気分安定薬臨床用量比，最終 ADHD 治療薬臨床用量比，最終抗認知症薬臨床用量比

<sup>a</sup>1 歳上がるごとの数値，<sup>b</sup>女性 1/男性 0，<sup>c</sup>1 回増えるごとの数値，<sup>d</sup>1 日増えるごとの数値，<sup>e</sup>1 上昇するごとの数値

Table 5: Factors associated with final prescription and laxative administration (using clinical dose ratio by category as explanatory variable)

Variable

B

S.E.

Wald

VIF

Odds ratio

95% CI

Lower limit

Upper limit

P

Age <sup>a</sup>

0.019 0.003 33.104 1.261 1.019 1.012 1.026 <0.001\*\*\*

Sex (female) <sup>b</sup>

	0.301	0.117	6.545	1.082	1.351	1.073	1.700	0.011*
Number of hospitalizations <sup>c</sup>								
	0.065	0.017	14.152	1.354	1.068	1.032	1.105	<0.001***
Length of stay on ward <sup>d</sup>								
	0.005	0.001	13.109	1.139	1.005	1.002	1.007	<0.001***
Final APD clinical dose ratio <sup>e</sup>								
	1.642	0.371	19.543	1.124	5.167	2.495	10.701	<0.001***
Final new antidepressant clinical dose ratio <sup>e</sup>								
	0.369	0.125	8.731	1.208	1.446	1.132	1.847	0.003**
Final conventional antidepressant clinical dose ratio <sup>e</sup>								
	1.934	0.554	12.193	1.026	6.918	2.336	20.487	<0.001**
Final mood stabilizer clinical dose ratio <sup>e</sup>								
	0.330	0.153	4.691	1.094	1.392	1.032	1.876	0.033*

Using the variable increment method. \*<0.05, \*\*<0.01, \*\*\*<0.001

Dependent variable: Use of laxatives in final prescription

Explanatory variables: Age, Sex (female), Living alone, Disability pension, Public assistance, Alcohol history, Smoking history, Treatment duration, Number of hospitalizations, Length of stay on ward, Isolation applied, Restraint applied, ECT applied, Final SGA clinical dose ratio, Final FGA clinical dose ratio, Final antipsychotic clinical dose ratio, Final new antidepressant clinical dose ratio, Final conventional antidepressant clinical dose ratio, Final BZD-type anxiolytic clinical dose ratio, Final BZD-type hypnotic clinical dose ratio, Final mood stabilizer clinical dose ratio, Final ADHD treatment clinical dose ratio, Final anti-dementia drug clinical dose ratio

<sup>a</sup> Value per 1-year increase, <sup>b</sup> Female 1/Male 0, <sup>c</sup> Value per additional instance, <sup>d</sup> Value per additional day, <sup>e</sup> Value per increase

表6 最終処方・抗精神病薬の処方率の比較（1例以上処方のあったもの）

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
アセナピン	55 (3.2%)	26 (3.8%)	29 (2.9%)	N.S.
アリピプラゾール	294 (17.3%)	129 (18.7%)	165 (16.4%)	N.S.
オランザピン	310 (18.3%)	119 (17.2%)	191 (19.0%)	N.S.
クエチアピン	264 (15.6%)	124 (17.9%)	140 (13.9%)	0.025*
パリペリドン	51 (3.0%)	22 (3.2%)	29 (2.9%)	N.S.
プレクスピプラゾール	58 (3.4%)	22 (3.2%)	36 (3.6%)	N.S.
プロナンセリン	55 (3.2%)	19 (2.7%)	36 (3.6%)	N.S.
プロナンセリンテープ	30 (1.8%)	10 (1.4%)	20 (2.0%)	N.S.
ペロスピロン	51 (3.0%)	21 (3.0%)	30 (3.0%)	N.S.
リスペリドン	243 (14.3%)	90 (13.0%)	153 (15.2%)	N.S.
ルラシドン	13 (0.8%)	8 (1.2%)	5 (0.5%)	N.S.
アリピプラゾール LAI	20 (1.2%)	9 (1.3%)	11 (1.1%)	N.S.
パリペリドン LAI	28 (1.7%)	9 (1.3%)	19 (1.9%)	N.S.
リスペリドン LAI	4 (0.2%)	0 (0.0%)	4 (0.4%)	N.S.
クロルプロマジン	55 (3.2%)	32 (4.6%)	23 (2.3%)	0.007**
スルトプリド	2 (0.1%)	2 (0.3%)	0 (0.0%)	N.S.
スルピリド	6 (0.4%)	0 (0.0%)	6 (0.6%)	0.041*
ゾテピン	21 (1.2%)	11 (1.6%)	10 (1.0%)	N.S.
チアプリド	1 (0.1%)	0 (0.0%)	1 (0.1%)	N.S.
ハロペリドール	34 (2.0%)	19 (2.7%)	15 (1.5%)	N.S.
プロペリシアジン	1 (0.1%)	1 (0.1%)	0 (0.0%)	N.S.
プロムペリドール	8 (0.5%)	1 (0.1%)	7 (0.7%)	N.S.
ペルフェナジン	1 (0.1%)	0 (0.0%)	1 (0.1%)	N.S.
レボメプロマジン	209 (12.3%)	106 (15.3%)	103 (10.2%)	0.002**
ハロペリドール LAI	2 (0.1%)	1 (0.1%)	1 (0.1%)	N.S.
フルフェナジン LAI	3 (0.2%)	2 (0.3%)	1 (0.1%)	N.S.

\* <0.05, \*\* <0.01

緩下剤あり群・緩下剤なし群の比較において、 $\chi^2$ 検定を用いた。処方5例以下の薬剤の比較については Fisher の正確確率検定を用いた。LAI：持効性注射薬

Table 6: Comparison of final prescriptions and antipsychotic prescription rates (for those with at least one prescription)

Total (n=1,696)

Laxative-prescribed group (n=691)

Non-laxative group (n=1,005)

P

Acenapine      55 (3.2%)      26 (3.8%)      29 (2.9%)      N.S.

Aripiprazole	294 (17.3%)	129 (18.7%)	165 (16.4%)	N.S.
Olanzapine	310 (18.3%)	119 (17.2%)	191 (19.0%)	N.S.
Quetiapine	264 (15.6%)	124 (17.9%)	140 (13.9%)	0.025*
Paliperidone	51 (3.0%)	22 (3.2%)	29 (2.9%)	N.S.
Brevipiprazole	58 (3.4%)	22 (3.2%)	36 (3.6%)	N.S.
Brolinancerin	55 (3.2%)	19 (2.7%)	36 (3.6%)	N.S.
Brolinancerin tape	30 (1.8%)	10 (1.4%)	20 (2.0%)	N.S.
Perospirone	51 (3.0%)	21 (3.0%)	30 (3.0%)	N.S.
Risperidone	243 (14.3%)	90 (13.0%)	153 (15.2%)	N.S.
Lurasidone	13 (0.8%)	8 (1.2%)	5 (0.5%)	N.S.
Aripiprazole LAI	20 (1.2%)	9 (1.3%)	11 (1.1%)	N.S.
Paliperidone LAI	28 (1.7%)	9 (1.3%)	19 (1.9%)	N.S.
Risperidone LAI	4 (0.2%)	0 (0.0%)	4 (0.4%)	N.S.
Chlorpromazine	55 (3.2%)	32 (4.6%)	23 (2.3%)	0.007**
Sulpiride	2 (0.1%)	2 (0.3%)	0 (0.0%)	N.S.
Sulpiride	6 (0.4%)	0 (0.0%)	6 (0.6%)	0.041*
Zotepine	21 (1.2%)	11 (1.6%)	10 (1.0%)	N.S.
Chiapid	1 (0.1%)	0 (0.0%)	1 (0.1%)	N.S.
Haloperidol	34 (2.0%)	19 (2.7%)	15 (1.5%)	N.S.
Propericiazine	1 (0.1%)	1 (0.1%)	0 (0.0%)	N.S.
Bromperidol	8 (0.5%)	1 (0.1%)	7 (0.7%)	N.S.
Perphenazine	1 (0.1%)	0 (0.0%)	1 (0.1%)	N.S.
Levomepromazine	209 (12.3%)	106 (15.3%)	103 (10.2%)	0.002**
Haloperidol LAI	2 (0.1%)	1 (0.1%)	1 (0.1%)	N.S.
Fluphenazine LAI	3 (0.2%)	2 (0.3%)	1 (0.1%)	N.S.

\* $<0.05$ , \*\* $<0.01$

For comparisons between the laxative-prescribed and non-laxative groups, the chi-square test was used. For comparisons of drugs with 5 or fewer prescriptions, Fisher's exact probability test was used. LAI: Long-acting injectable

表7 最終処方・新規抗うつ薬と気分安定薬（クエチアピン徐放錠を含む）の処方率の比較（1例以上処方のあったもの）

	全体 (n=1,696)	緩下剤あり (n=691)	緩下剤なし (n=1,005)	P
エスシタロプラム	55 (3.2%)	23 (3.3%)	32 (3.2%)	N.S.
セルトラリン	14 (0.8%)	6 (0.9%)	8 (0.8%)	N.S.
パロキセチン	13 (0.8%)	7 (1.0%)	6 (0.6%)	N.S.
パロキセチン (徐放錠)	21 (1.2%)	7 (1.0%)	14 (1.4%)	N.S.
ボルチオキセチン	10 (0.6%)	8 (1.2%)	2 (0.2%)	0.011*
フルボキサミン	21 (1.2%)	6 (0.9%)	15 (1.5%)	N.S.
デュロキセチン	70 (4.1%)	38 (5.5%)	32 (3.2%)	0.018*
ベンラファキシン	24 (1.4%)	18 (2.6%)	6 (0.6%)	<0.001***
ミルタザピン	160 (9.4%)	96 (13.9%)	64 (6.4%)	<0.001***
カルバマゼピン	40 (2.4%)	21 (3.0%)	19 (1.9%)	N.S.
パルプロ酸	425 (25.1%)	159 (23.0%)	266 (26.5%)	N.S.
ラモトリギン	125 (7.4%)	67 (9.7%)	58 (5.8%)	0.002**
炭酸リチウム	119 (7.0%)	59 (8.5%)	60 (6.0%)	0.041*
クエチアピン (徐放錠)	44 (2.6%)	29 (4.2%)	15 (1.5%)	<0.001***

\* <0.05, \*\* <0.01, \*\*\* <0.001

緩下剤あり群・緩下剤なし群の比較において、 $\chi^2$ 検定を用いた。処方5例以下の薬剤の比較についてはFisherの正確確率検定を用いた。

Table 7: Comparison of prescription rates for final prescriptions, new antidepressants, and mood stabilizers (including quetiapine extended-release tablets) (for drugs prescribed in at least 1 case)

Total (n=1,696)

Laxative-prescribed group (n=691)

Non-laxative group (n=1,005)

P

Escitalopram	55 (3.2%)	23 (3.3%)	32 (3.2%)	N.S.
Sertraline	14 (0.8%)	6 (0.9%)	8 (0.8%)	N.S.
Paroxetine	13 (0.8%)	7 (1.0%)	6 (0.6%)	N.S.
Paroxetine (extended-release tablets)	21 (1.2%)	7 (1.0%)	14 (1.4%)	N.S.
Vortioxetine	10 (0.6%)	8 (1.2%)	2 (0.2%)	0.011*
Fluvoxamine	21 (1.2%)	6 (0.9%)	15 (1.5%)	N.S.
Duloxetine	70 (4.1%)	38 (5.5%)	32 (3.2%)	0.018*

Venlafaxine	24 (1.4%)	18 (2.6%)	6 (0.6%)	<0.001***
Mirtazapine	160 (9.4%)	96 (13.9%)	64 (6.4%)	<0.001***
Carbamazepine	40 (2.4%)	21 (3.0%)	19 (1.9%)	N.S.
Valproic acid	425 (25.1%)	159 (23.0%)	266 (26.5%)	N.S.
Lamotrigine	125 (7.4%)	67 (9.7%)	58 (5.8%)	0.002**
Lithium carbonate				
	119 (7.0%)	59 (8.5%)	60 (6.0%)	0.041*
Quetiapine (extended-release tablets)				
	44 (2.6%)	29 (4.2%)	15 (1.5%)	<0.001***

\*<0.05, \*\*<0.01, \*\*\*<0.001

The  $\chi^2$  test was used to compare the laxative-prescribed and non-laxative groups. Fisher's exact test was used for comparisons involving drugs with five or fewer prescriptions.

表 8 最終処方・緩下剤投与ありに関連する因子（抗精神病薬・新規抗うつ薬・気分安定薬について薬剤別の臨床用量比を説明変数としたもの）

	B	S.E	Wald	VIF	Odds ratio	95% CI		P
						下限	上限	
年齢 <sup>a</sup>	0.019	0.003	33.018	1.317	1.019	1.013	1.026	<0.001***
性別 <sup>b</sup>	0.304	0.119	6.519	1.132	1.356	1.073	1.713	0.011*
入院回数 <sup>c</sup>	0.061	0.018	11.731	1.568	1.063	1.026	1.101	0.001**
在棟日数 <sup>d</sup>	0.004	0.001	10.632	1.198	1.004	1.002	1.007	0.001**
クエチアピン 臨床用量比 <sup>e</sup>	1.054	0.391	7.259	1.140	2.870	1.333	6.179	0.007**
レボメプロマジン 臨床用量比 <sup>e</sup>	1.246	0.456	7.477	1.128	3.475	1.423	8.485	0.006**
抗パ薬 臨床用量比 <sup>e</sup>	1.466	0.376	15.228	1.229	4.333	2.075	9.049	<0.001***
ベンラファキシン 臨床用量比 <sup>e</sup>	1.788	0.655	7.460	1.025	5.977	1.657	21.561	0.006**
ミルタザピン 臨床用量比 <sup>e</sup>	0.927	0.234	15.655	1.164	2.526	1.596	3.998	<0.001***
従来型抗うつ薬 臨床用量比 <sup>e</sup>	1.875	0.553	11.502	1.054	6.524	2.207	19.284	0.001**
BZD系睡眠薬 臨床用量比 <sup>e</sup>	0.162	0.08	4.049	1.123	1.176	1.004	1.376	0.044*
クエチアピン (徐放錠) 臨床用量比 <sup>e</sup>	1.706	0.522	10.690	1.054	5.504	1.980	15.302	0.001**

変数増加法による。\* < 0.05, \*\* < 0.01, \*\*\* < 0.001

目的変数：最終処方での緩下剤使用あり

説明変数：年齢，性別（女性），単身生活，障害年金，生活保護，飲酒歴，喫煙歴，治療期間，入院回数，在棟日数，隔離施行，拘束施行，ECT 施行，最終 SGA，FGA 臨床用量比（表 6，薬剤別），最終抗パ薬臨床用量比，最終新規抗うつ薬臨床用量比（表 7，薬剤別），最終従来型抗うつ薬臨床用量比，最終 BZD 系抗不安薬臨床用量比，最終 BZD 系睡眠薬臨床用量比，最終気分安定薬臨床用量比（表 7，薬剤別），最終 ADHD 治療薬臨床用量比，最終抗認知症薬臨床用量比

<sup>a</sup>1 歳上がるごとの数値，<sup>b</sup>女性 1/男性 0，<sup>c</sup>1 回増えるごとの数値，<sup>d</sup>1 日増えるごとの数値，<sup>e</sup>1 上昇するごとの数値

Table 8: Factors associated with final prescription and laxative administration (using clinical dose ratios by drug type for antipsychotics, new antidepressants, and mood stabilizers as explanatory variables)

B

S.E.

Wald

VIF

Odds ratio

95% CI

Lower limit Upper limit

*P*

Age <sup>a</sup>	0.019	0.003	33.018	1.317	1.019	1.013	1.026	<0.001***
Sex <sup>b</sup>	0.304	0.119	6.519	1.132	1.356	1.073	1.713	0.011*
Number of hospitalizations <sup>c</sup>	0.061	0.018	11.731	1.568	1.063	1.026	1.101	0.001**
Length of stay on ward <sup>d</sup>	0.004	0.001	10.632	1.198	1.004	1.002	1.007	0.001**
Clinical dose ratio <sup>e</sup> of quetiapine	1.054	0.391	7.259	1.140	2.870	1.333	6.179	0.007**
Clinical dose ratio <sup>e</sup> of levomepromazine	1.246	0.456	7.477	1.128	3.475	1.423	8.485	0.006**
Clinical dose ratio <sup>e</sup> of APDs	1.466	0.376	15.228	1.229	4.333	2.075	9.049	<0.001***
Clinical dose ratio <sup>e</sup> of venlafaxine	1.788	0.655	7.460	1.025	5.977	1.657	21.561	0.006**
Clinical dose ratio <sup>e</sup> of mirtazapine	0.927	0.234	15.655	1.164	2.526	1.596	3.998	<0.001***
Clinical dose ratio <sup>e</sup> of conventional antidepressants	1.875	0.553	11.502	1.054	6.524	2.207	19.284	0.001**
Clinical dose ratio <sup>e</sup> of BZD sleep medications	0.162	0.08	4.049	1.123	1.176	1.004	1.376	0.044*
Clinical dose ratio <sup>e</sup> of quetiapine (extended-release tablets)	1.706	0.522	10.690	1.054	5.504	1.980	15.302	0.001**

\*<0.05, \*\*<0.01, \*\*\*<0.001

Dependent variable: Use of laxatives in final prescription

Explanatory variables: Age, Sex (female), Living alone, Disability pension, Public assistance, Alcohol history, Smoking history, Treatment duration, Number of hospitalizations, Days on ward, Isolation implemented, Restraint application, ECT application, Final SGA, FGA clinical dose ratio (Table 6, by drug), Final antipsychotic clinical dose ratio, Final new antidepressant clinical dose ratio (Table 7, by drug), Final conventional antidepressant clinical dose ratio, Final BZD-type anxiolytic clinical dose ratio, Final BZD-type hypnotic clinical dose ratio, Final mood

stabilizer clinical dose ratio (Table 7, by drug), Final ADHD treatment drug clinical dose ratio, final anti-dementia drug clinical dose ratio

<sup>a</sup> Value per year of age increase, <sup>b</sup> Female 1/Male 0, <sup>c</sup> Value per additional dose, <sup>d</sup> Value per additional day, <sup>e</sup> Value per increase